Shahnan-Shah
10/729027


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     FILE 'REGISTRY' ENTERED AT 14:58:00 ON 25 AUG 2004
                E ADIPIC ACID DIHYDRAZIDE/CN 5
                E "E-AMINOHEXANOIC ACID"/CN 5
L1              1 S E3
L2              1 S 1071-93-8/RN
                E CHLOROHEXANOL DIMETHYL ACETAL/CN 5
                E "D-GLUCURONOLACTONE"/CN 5
L3              1 S E3
                E "P-NITROPHENYLETHYL AMINE"/CN 5
L4              1 S 24954-67-4/RN
L5              4 S L1 OR L2 OR L3 OR L4

     FILE 'CAPLUS' ENTERED AT 15:15:15 ON 25 AUG 2004
L1              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "E-AMINOHEXANOIC
                  ACID"/CN
L2              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  1071-93-8/RN
L3              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  D-GLUCURONOLACTONE/CN
L4              1 SEA FILE=REGISTRY ABB=ON  PLU=ON  24954-67-4/RN
L5              4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4
L6           1726 SEA FILE=CAPLUS ABB=ON  PLU=ON  (MORAXELL? OR M OR BRANHAMELL?
                  OR B)(W)CATARRHAL?
L7           6684 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 OR ADIPIC(1W)(DIHYDRAZIDE
                  OR DI HYDRAZIDE) OR EPSILON(W)(AMINOHEXANOIC OR AMINO HEXANOIC)
                   OR (CHLOROHEXANOL OR CHLORO HEXANOL)(W)(DIMETHYL? OR DI(W)(MET
                  HYL? OR ME)) OR D(W)(GLUCURONOLACTONE OR GLUCURONO LACTONE)
L8            565 SEA FILE=CAPLUS ABB=ON  PLU=ON  P(W)(NITROPHENYLETHYL? OR
                  NITRO(W)(PHENYLETHYL? OR (PH OR PHENYL)(W)(ETHYL? OR ET)) OR
                  NITROPHENYL ETHYL?)
L9              3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND (L7 OR L8)

L9   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
ED   Entered STN:  22 Sep 1999
ACCESSION NUMBER:         1999:597423  CAPLUS
DOCUMENT NUMBER:          131:213104
TITLE:                    Antigenic conjugates of conserved lipopolysaccharides
                          of gram negative bacteria
INVENTOR(S):              Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella,
                          Michael A.; Gibson, Bradford W.
PATENT ASSIGNEE(S):       American Cyanamid Company, USA
SOURCE:                   Eur. Pat. Appl., 18 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     EP 941738             A1    19990915    EP 1999-301747          19990309
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     CA 2264970            AA    19990910    CA 1999-2264970         19990308
     AU 9919540            A1    19990923    AU 1999-19540           19990309
     AU 766184             B2    20031009
     JP 11322793           A2    19991124    JP 1999-61354           19990309
     BR 9902008            A     20000509    BR 1999-2008            19990309
```

Searcher : Shears 571-272-2528

-key terms
adipic acid dihydrazide
date not given

PRIORITY APPLN. INFO.: US 1998-37529 A 19980310

AB Antigenic conjugates are provided which comprise a carrier protein covalently bonded to the conserved portion of a lipopolysaccharide of a gram neg. bacteria, wherein said conserved portion of the lipopolysaccharide comprises the inner core and lipid A portions of said lipopolysaccharide, said conjugate eliciting a cross reactive immune response against heterologous strains of said gram neg. bacteria. The carrier protein is selected from CRM197, tetanus toxin, diphtheria toxin, pseudomonas exotoxin A, cholera toxin, group A streptococcal toxin, pneumolysin of Streptococcus pneumoniae, filamentous hemagglutinin (FHA), FHA of Bordetella pertussis, pili or pilins of Neisseria gonorrhoeae or meningitidis, outer membrane proteins of Neisseria meningitidis, C5A peptidase of Streptococcus and surface protein of **Moraxella catarrhalis.**

IT **1071-93-8, Adipic** acid **dihydrazide**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker; conjugates of conserved lipopolysaccharides of gram neg. bacteria and carrier proteins for eliciting cross reactive immune response against heterologous strains of gram neg. bacteria)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

data not good.

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 Jul 1999
ACCESSION NUMBER: 1999:464181 CAPLUS
DOCUMENT NUMBER: 131:86860
TITLE: Lipooligosaccharide-based vaccine for prevention of Moraxella (**Branhamella**) **catarrhalis** infections in mammals
INVENTOR(S): Gu, Xin-Xing; Robbins, John B.
PATENT ASSIGNEE(S): The Government of the United States of America, Department of Health and Human, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936086	A1	19990722	WO 1999-US590	19990112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315746	AA	19990722	CA 1999-2315746	19990112
AU 9922212	A1	19990802	AU 1999-22212	19990112
BR 9906902	A	20001017	BR 1999-6902	19990112
EP 1047447	A1	20001102	EP 1999-902170	19990112

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002509115	T2	20020326	JP 2000-539859	19990112
US 6685949	B1	20040203	US 2000-610034	20000705
US 2004126381	A1	20040701	US 2003-688115	20031017
US 2004115214	A1	20040617	US 2003-729027	20031205
PRIORITY APPLN. INFO.:			US 1998-71483P	P 19980113
			US 1996-16020P	P 19960423
			US 1997-842409	A3 19970423
			WO 1999-US590	W 19990112
			US 2000-610034	A2 20000705
			US 2001-789017	A2 20010220
			US 2001-288695P	P 20010503
			WO 2001-US32331	A1 20011016

AB A conjugate vaccine for **Moraxella catarrhalis** comprising isolated lipooligosaccharide from which esterified fatty acids have been removed, to produce a detoxified lipooligosaccharide (dLOS), or from which lipid A has been removed, to produce a detoxified oligosaccharide (OS), which is linked to an immunogenic carrier. The immunogenic carrier is selected from the group consisting of UspA or CD derived from **M. catarrhalis**, tetanus toxoid, HMP derived from Haemophilus influenza, diphtheria toxoid, detoxified P. aeruginosa toxin A, cholera toxin, pertussis toxin, hepatitis B surface or core antigen, rotavirus VP 7 protein, CRM, CRM197, CRM3201 and respiratory syncytial virus F and G protein. The vaccine is useful for preventing otitis media and respiratory infections caused by **M. catarrhalis** in mammals, including humans.

IT **60-32-2**, ε-**Aminohexanoic** acid
1071-93-8, **Adipic** acid **dihydrazide**
24954-67-4, **p-Nitrophenylethyl** amine
32449-92-6, **D-Glucuronolactone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker; lipooligosaccharide-based vaccine for prevention of Moraxella (**Branhamella**) **catarrhalis** infections in mammals)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 21 May 1998
ACCESSION NUMBER: 1998:296912 CAPLUS
DOCUMENT NUMBER: 129:53186
TITLE: Synthesis and characterization of lipooligosaccharide-based conjugates as vaccine candidates for Moraxella (**Branhamella**) **catarrhalis**
AUTHOR(S): Gu, Xin-Xing; Chen, Jing; Barenkamp, Stephen J.; Robbins, John B.; Tsai, Chao-Ming; Lim, David J.; Battey, James
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA
SOURCE: Infection and Immunity (1998), 66(5), 1891-1897
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Moraxella (**Branhamella**) **catarrhalis** is an important

cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults. Lipooligosaccharide (LOS) is a major surface antigen of the bacterium and elicits bactericidal antibodies. Treatment of the LOS from strain ATCC 25238 with anhydrous hydrazine reduced its toxicity 20,000-fold, as assayed in the Limulus amebocyte lysate (LAL) test. The detoxified LOS (dLOS) was coupled to tetanus toxoid (TT) or high-mol.-weight proteins (HMP) from nontypeable Haemophilus influenzae through a linker of **adipic** acid **dihydrazide** to form dLOS-TT or dLOS-HMP. The molar ratios of dLOS to TT and HMP conjugates were 19:1 and 31:1, resp. The antigenicity of the two conjugates was similar to that of the LOS, as determined by double immunodiffusion. S.c. or i.m. injection of both conjugates elicited a 50- to 100-fold rise in the geometric mean of IgG to the homologous LOS in mice after three injections and a 350- to 700-fold rise of anti-LOS IgG in rabbits after two injections. The immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of **M. catarrhalis**. These results indicate that a detoxified LOS-protein conjugate is a candidate for immunization against **M. catarrhalis** diseases.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:22:35 ON 25 AUG 2004)

L10 6 S L9
L11 3 DUP REM L10 (3 DUPLICATES REMOVED)

L11 ANSWER 1 OF 3 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1999-444322 [37] WPIDS
CROSS REFERENCE: 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]; 2004-516882 [49]
DOC. NO. CPI: C1999-130893
TITLE: Detoxified lipooligosaccharide-based vaccine for prevention of **Moraxella catarrhalis** infections in mammals.
DERWENT CLASS: B04 D16
INVENTOR(S): GU, X; ROBBINS, J B
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (GUXX-I) GU X; (ROBB-I) ROBBINS J B
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9936086	A1	19990722	(199937)*	EN	60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9922212	A	19990802	(199954)		
BR 9906902	A	20001017	(200056)		

EP 1047447	A1	20001102	(200056)	EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE				
CN 1288384	A	20010321	(200137)	
KR 2001034124	A	20010425	(200164)	
MX 2000006678	A1	20010201	(200168)	
JP 2002509115	W	20020326	(200236)	66
US 6685949	B1	20040203	(200413)	
US 2004115214	A1	20040617	(200440)	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9936086	A1		WO 1999-US590	19990112
AU 9922212	A		AU 1999-22212	19990112
BR 9906902	A		BR 1999-6902	19990112
			WO 1999-US590	19990112
EP 1047447	A1		EP 1999-902170	19990112
			WO 1999-US590	19990112
CN 1288384	A		CN 1999-802142	19990112
KR 2001034124	A		KR 2000-707737	20000713
MX 2000006678	A1		MX 2000-6678	20000706
JP 2002509115	W		WO 1999-US590	19990112
			JP 2000-539859	19990112
US 6685949	B1	Provisional	US 1998-71483P	19980113
		Cont of	WO 1999-US590	19990112
			US 2000-610034	20000705
US 2004115214	A1	Provisional	US 1998-71483P	19980113
		Cont of	WO 1999-US590	19990112
		Div ex	US 2000-610034	20000705
			US 2003-729027	20031205

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9922212	A	Based on	WO 9936086
BR 9906902	A	Based on	WO 9936086
EP 1047447	A1	Based on	WO 9936086
JP 2002509115	W	Based on	WO 9936086
US 2004115214	A1	Div ex	US 6685949

PRIORITY APPLN. INFO: US 1998-71483P 19980113; US 2000-610034 20000705; US 2003-729027 20031205

AN 1999-444322 [37] WPIDS

CR 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]; 2004-516882 [49]

AB WO 9936086 A UPAB: 20040802

NOVELTY - A lipooligosaccharide (LOS) isolated from **Moraxella catarrhalis** and detoxified by removal of ester-linked fatty acids to produce detoxified LOS (dLOS) or treated to remove lipid A to produce oligosaccharide (OS) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for a conjugate vaccine for **M. catarrhalis** comprising dLOS or OS, and a covalently linked immunogenic carrier as above; methods of detoxifying LOS isolated from **M. catarrhalis**, by

removal of ester-linked fatty acids; methods of making a conjugate vaccine as above.

ACTIVITY - Immunoprotective; Auditory; Antibacterial.

MECHANISM OF ACTION - Vaccine.

USE - The methods are useful for isolation of detoxified lipooligosaccharide or oligosaccharide from **M. catarrhalis**. The detoxified lipooligosaccharide or oligosaccharide are useful in conjugate vaccines. The vaccine is useful for protection against **M. catarrhalis** which causes otitis media and respiratory infections.

ADVANTAGE - The invention provides a detoxified lipooligosaccharide from **M. catarrhalis**, the major virulence factor for pathogenesis of bacterial infections. When tested by the standard Limulus amebocyte lysate assay, the isolated LOS showed 2 x 104 EU/ mu g, whereas the dLOS showed 1 EU/ mu g, representing a 20000-fold reduction of toxicity.

Dwg.0/3

L11 ANSWER 2 OF 3 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1999-495801 [42] WPIDS

DOC. NO. CPI: C1999-145508

TITLE: New antigenic conjugates from bacteria, useful as vaccines.

DERWENT CLASS: B04 D16

INVENTOR(S): APICELLA, M A; ARUMUGHAM, R G; FORTUNA-NEVIN, M; GIBSON, B W

PATENT ASSIGNEE(S): (AMHP) WYETH HOLDINGS CORP; (AMCY) AMERICAN CYANAMID CO

COUNTRY COUNT: 31

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 941738	A1	19990915	(199942)*	EN	17
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 9919540	A	19990923	(199951)		
CA 2264970	A1	19990910	(200006)	EN	
JP 11322793	A	19991124	(200006)		18
BR 9902008	A	20000509	(200033)		
KR 99077705	A	19991025	(200052)		
AU 766184	B	20031009	(200373)		
US 6645503	B1	20031111	(200382)#		
US 2004052804	A1	20040318	(200421)#		
AU 2004200060	A1	20040129	(200443)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 941738	A1	EP 1999-301747	19990309
AU 9919540	A	AU 1999-19540	19990309
CA 2264970	A1	CA 1999-2264970	19990308
JP 11322793	A	JP 1999-61354	19990309
BR 9902008	A	BR 1999-2008	19990309
KR 99077705	A	KR 1999-7668	19990309
AU 766184	B	AU 1999-19540	19990309

US 6645503	B1 Provisional	US 1998-88364P	19980310
		US 1999-264747	19990309
US 2004052804	A1 Provisional Div ex	US 1998-88364P	19980310
		US 1999-264747	19990309
		US 2003-643314	20030819
AU 2004200060	A1	AU 2004-200060	20040107

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 766184	B Previous Publ.	AU 9919540
US 2004052804	A1 Div ex	US 6645503
AU 2004200060	A1 Div ex	AU 766184

PRIORITY APPLN. INFO: US 1998-37529 19980310; US 1999-264747 19990309; US 2003-643314 20030819; AU 2004-200060 20040107

AN 1999-495801 [42] WPIDS

AB EP 941738 A UPAB: 19991014

NOVELTY - An antigenic conjugate (I) comprising a carrier protein covalently bonded to the conserved portion of a lipopolysaccharide (LPS) of a gram negative bacteria is new. The conserved portion comprises the inner core and lipid A regions of the LPS and the conjugate elicits a cross reactive immune response against heterologous strains of gram negative bacteria.

ACTIVITY - None given.

MECHANISM OF ACTION - Vaccine.

USE - (I) may be administered to patients as a prophylactic vaccine against Neisseria gonorrhoeae, Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella minnesota, Proteus mirabilis, Pseudomonas aeruginosa, **Moraxella catarrhalis,** Bordetella pertussis, Shigella, Klebsiella and Vibrio cholerae, especially Neisseria meningitidis which produce LPS (claimed). These vaccines may be used to prevent bacterial sepsis. Antibodies generated by these vaccines may be used to examine whether an infection has been caused by an LPS-producing organism by testing blood samples, body fluids or biopsy materials of infected individuals. These antibodies may also be directly administered to patients as prophylactic agents against the bacteria listed above.

ADVANTAGE - (I) induces a cross-reactive and cross-functional antibody response against heterologous strains of gram negative bacteria. In contrast prior art LPS vaccines were restricted in the number of strains they protected against.

Dwg.0/4

L11 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1998234010 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9573066

TITLE: Synthesis and characterization of lipooligosaccharide-based conjugates as vaccine candidates for Moraxella (**Branhamella**) **catarrhalis.**

AUTHOR: Gu X X; Chen J; Barenkamp S J; Robbins J B; Tsai C M; Lim D J; Battey J

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, Rockville, Maryland 20850, USA.. xgu@pop.nidcd.nih.gov
SOURCE: Infection and immunity, (1998 May) 66 (5) 1891-7. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980514

AB Moraxella (**Branhamella**) **catarrhalis** is an important cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults. Lipooligosaccharide (LOS) is a major surface antigen of the bacterium and elicits bactericidal antibodies. Treatment of the LOS from strain ATCC 25238 with anhydrous hydrazine reduced its toxicity 20,000-fold, as assayed in the Limulus amebocyte lysate (LAL) test. The detoxified LOS (dLOS) was coupled to tetanus toxoid (TT) or high-molecular-weight proteins (HMP) from nontypeable Haemophilus influenzae through a linker of **adipic** acid **dihydrazide** to form dLOS-TT or dLOS-HMP. The molar ratios of dLOS to TT and HMP conjugates were 19:1 and 31:1, respectively. The antigenicity of the two conjugates was similar to that of the LOS, as determined by double immunodiffusion. Subcutaneous or intramuscular injection of both conjugates elicited a 50- to 100-fold rise in the geometric mean of immunoglobulin G (IgG) to the homologous LOS in mice after three injections and a 350- to 700-fold rise of anti-LOS IgG in rabbits after two injections. The immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of **M. catarrhalis**. These results indicate that a detoxified LOS-protein conjugate is a candidate for immunization against **M. catarrhalis** diseases.

(FILE 'REGISTRY' ENTERED AT 15:30:27 ON 25 AUG 2004)
E MONOPHOSPHORYL LIPID A/CN 5
L14 2 S E3
E TREHALOSE DIMYCOLATE/CN 5
E "TREHALOSE, DIMYCOLATE"/CN 5
E TREHALOSE/CN 5
L15 1 S E3
E ALUM/CN 5
L16 2 S E3
L17 5 S L14 OR L15 OR L16

FILE 'CAPLUS' ENTERED AT 15:32:26 ON 25 AUG 2004
L6 1726 SEA FILE=CAPLUS ABB=ON PLU=ON (MORAXELL? OR M OR BRANHAMELL? OR B)(W)CATARRHAL?
L12 47 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (DLOS OR LOS OR LIPOOLIGOSACCHARIDE OR OLIGOSACCHARIDE OR OLIGO SACCHARIDE OR LIPOOLIGO SACCHARIDE OR OS)
L13 28 SEA FILE=CAPLUS ABB=ON PLU=ON L12 AND (USPA OR USP A OR CD OR TOXIN OR TOXOID OR DT OR HMP OR HIGH MOL?(1W)PROTEIN OR

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                ANTIGEN OR VP7 OR VP 7 OR CRM? OR RSV# OR RESPIRATOR? SYNCYT?
                VIRUS)
L14         2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "MONOPHOSPHORYL LIPID A"/CN
L15         1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TREHALOSE/CN
L16         2 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALUM/CN
L17         5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 OR L15 OR L16
L18         9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND (L17 OR LIPID A OR
                TREHALOSE OR ALUM)


L19         7 L18 NOT L9

L19  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
ED   Entered STN:  22 Feb 2004
ACCESSION NUMBER:          2004:142987  CAPLUS
DOCUMENT NUMBER:           140:180124
TITLE:                     Engineered meningococcal strains comprising
                           LOS subunit or outer membrane vesicle with
                           downregulated or deleted PorA, OpA and/or OpC for use
                           as neisserial vaccines
INVENTOR(S):               Biemans, Ralph; Denoel, Philippe; Feron, Christiane;
                           Goraj, Karine; Poolman, Jan; Weynants, Vincent
PATENT ASSIGNEE(S):        Glaxosmithkline Biologicals SA, Belg.
SOURCE:                    PCT Int. Appl., 51 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    6
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ----------            ----   --------    --------------------     --------
     WO 2004014417          A2    20040219    WO 2003-EP8568           20030731
     WO 2004014417          A3    20040722
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       GB 2002-18035      A  20020802
                                             GB 2002-18036      A  20020802
                                             GB 2002-18037      A  20020802
                                             GB 2002-18051      A  20020802
                                             GB 2002-20197      A  20020830
                                             GB 2002-20199      A  20020830
                                             GB 2002-25524      A  20021101
                                             GB 2002-25531      A  20021101
                                             GB 2002-30164      A  20021224
                                             GB 2002-30168      A  20021224
                                             GB 2002-30170      A  20021224
```

GB 2003-5028 A 20030305

AB The present invention relates to the field of neisserial vaccine compns., their manufacture, and the use of such compns. in medicine. More particularly
it relates to processes of making novel engineered meningococcal strains which are more suitable for the production of neisserial, in particular meningococcal, outer-membrane vesicle (or bleb) vaccines. Advantageous processes and vaccine products are also described based on the use of novel **LOS** subunit or meningococcal outer-membrane vesicle (or bleb) vaccines which have been rendered safer and/or more effective for use in human subjects. In particular combinations of gene downregulations are described such as PorA & OpA, PorA and OpC, OpA and OpC, and PorA and OpA and OpC; as well as gene upregulations are describe such as NspA, TbpA low, TbpA high, Hsf, Hap, OMP85, PilQ, NadA, LbpA, and MltA. Alternatively, or in addition, lgtB- is shown to be an optimal mutation for effectively and safely using L3 and/or L2 **LOS** in Neisseria vaccine compns. Bleb vaccines derived from lgtB- and capsular polysaccharide deficient meningococcal mutants are further described; as are advantageous methods of making bleb prepns. where **LOS** is to be retained as an important **antigen.**

L19 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 Oct 2003
ACCESSION NUMBER: 2003:777114 CAPLUS
DOCUMENT NUMBER: 139:291102
TITLE: Immunogenic hepatitis B virus core chimeric particles stabilized with an N-terminal cysteine
INVENTOR(S): Birkett, Ashley J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 110 pp., Cont.-in-part of U.S. Ser. No. 930,915.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003185858	A1	20031002	US 2002-82014	20020221
US 2003138769	A1	20030724	US 2001-930915	20010815
US 2003198645	A1	20031023	US 2003-372076	20030221
WO 2003102165	A2	20031211	WO 2003-US5196	20030221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004156863	A1	20040812	US 2003-677074	20031001
US 2004146524	A1	20040729	US 2003-732862	20031210

PRIORITY APPLN. INFO.:	US 2001-930915	A2 20010815
	US 2000-225843P	P 20000816
	US 2000-226867P	P 20000822
	US 2002-80299	A2 20020221
	US 2002-82014	A2 20020221
	US 2002-274616	A 20021021
	US 2002-432123P	P 20021210
	US 2003-372076	A2 20030221

AB The author discloses chimeric, C-terminal truncated hepatitis B virus nucleocapsid protein (HBc) that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The immunogenic epitope is peptide-bonded to the N-terminus, in the immunogenic loop or at the C-terminus of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the N-terminus of the chimer mol. Methods of making and using the chimeras are also disclosed.

L19 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 07 Mar 2003
ACCESSION NUMBER: 2003:173462 CAPLUS
DOCUMENT NUMBER: 138:203668
TITLE: Helicobacter pylori vaccination
INVENTOR(S): Del Giudice, Giuseppe
PATENT ASSIGNEE(S): Chiron SpA, Italy
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018054	A1	20030306	WO 2002-IB3768	20020902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423142	A1	20040602	EP 2002-762721	20020902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:	GB 2001-21208	A 20010831
	GB 2001-25665	A 20011025
	GB 2002-5018	A 20020304
	WO 2002-IB3768	W 20020902

AB A sterile immunogenic preparation of three purified H.pylori **antigens** (CagA, VacA and NAP) adjuvanted with **alum** in an isotonic buffer solution for i.m. injection is discussed. The **antigens** may be administered in conjunction with antibiotics and/or antisecretories.

Urease breath testing, stool **antigen** testing, and/or immunol. anal. may be used as correlate(s) of protection against H.pylori infection. Urea may be used to improve VacA solubility

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Nov 2002
ACCESSION NUMBER: 2002:868765 CAPLUS
DOCUMENT NUMBER: 137:336726
TITLE: Intranasal immunization with detoxified **lipooligosaccharide** from nontypeable Haemophilus influenzae or **Moraxella catarrhalis**
INVENTOR(S): Gu, Xin-Xing
PATENT ASSIGNEE(S): United States, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002089839	A1	20021114	WO 2001-US32331	20011016
W: AU, CA, JP, US				
US 2004126381	A1	20040701	US 2003-688115	20031017

PRIORITY APPLN. INFO.:

US 2001-288695P	P	20010503
US 1996-16020P	P	19960423
US 1997-842409	A3	19970423
US 1998-71483P	P	19980113
WO 1999-US590	A1	19990112
US 2000-610034	A2	20000705
US 2001-789017	A2	20010220
WO 2001-US32331	A1	20011016

AB The invention relates to intranasal immunization with detoxified **lipooligosaccharide** from nontypeable Haemophilus influenzae or **Moraxella catarrhalis**. The detoxified **lipooligosaccharide** can be conjugated to an immunogenic carrier, such as tetanus **toxoid** or diphtheria **toxin**. The detoxified **lipooligosaccharide** is administered intranasally with an adjuvant or delivery system.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Feb 2002
ACCESSION NUMBER: 2002:142851 CAPLUS
DOCUMENT NUMBER: 136:215388
TITLE: Immunogenic hepatitis B nucleocapsid protein (HBc) chimeric particles having enhanced stability
INVENTOR(S): Birkett, Ashley J.
PATENT ASSIGNEE(S): Apovia, Inc., USA
SOURCE: PCT Int. Appl., 290 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014478	A2	20020221	WO 2001-US41759	20010816
WO 2002014478	A3	20030605		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003138769	A1	20030724	US 2001-930915	20010815
AU 2001085452	A5	20020225	AU 2001-85452	20010816
EP 1333857	A2	20030813	EP 2001-964615	20010816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004152876	A1	20040805	US 2004-806006	20040322
US 2004156864	A1	20040812	US 2004-805913	20040322

PRIORITY APPLN. INFO.:

US 2000-225843P	P	20000816
US 2000-226867P	P	20000822
US 2001-930915	A	20010815
WO 2001-US41759	W	20010816

AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (core protein or HBc) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The immunogenic epitope is a B cell epitope or T cell epitope derived from pathogen such as Streptococcus pneumonia, Cryptosporidium parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestia, etc. The display of the immunogenic epitope is displayed in the immunogenic loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed.

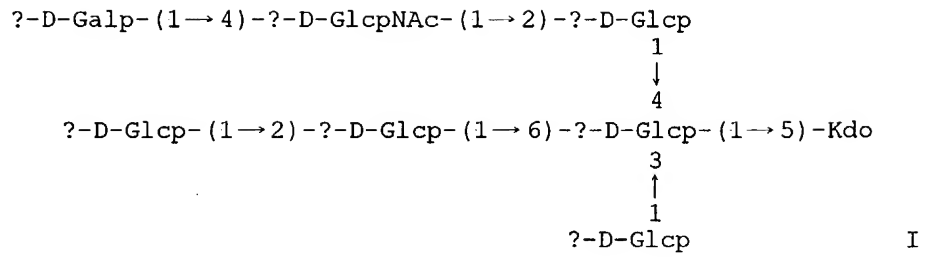
L19 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Dec 1998
ACCESSION NUMBER: 1998:800024 CAPLUS
DOCUMENT NUMBER: 130:51336
TITLE: Laft mutants of pathogenic gram-negative bacteria
INVENTOR(S): Apicella, Michael A.; Gibson, Bradford W.; Nichols, Wade A.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA; University of California
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853851	A1	19981203	WO 1998-US10881	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877010	A1	19981230	AU 1998-77010	19980528
PRIORITY APPLN. INFO.:			US 1997-47791P P	19970528
			WO 1998-US10881 W	19980528

AB A method is provided for identifying, isolating, and producing **lipooligosaccharide** (**LOS**) mutants of gram-neg. bacterial pathogens. The method comprises mutating the laft gene of a gram-neg. bacterial pathogen so that there is a lack of a functional **Lipid A** fatty acid transferase protein. The resulting **LOS** mutants lack one or more secondary acyl chains as compared to the **LOS** contained in the wild type gram-neg. bacterial pathogen. The **LOS** isolated from the laft mutants displays substantially reduced toxicity as compared to that of the wild type strain. Also, the present invention provides methods for using a vaccine formulation containing the laft mutants, the endotoxin isolated therefrom, or the endotoxin isolated therefrom which is then conjugated to a carrier protein, to immunize an individual against infections caused by gram-neg. bacterial pathogens by administering a prophylactically effective amount of the vaccine formulation.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Feb 1995
ACCESSION NUMBER: 1995:320431 CAPLUS
DOCUMENT NUMBER: 122:240278
TITLE: Structural studies of the O-**antigen oligosaccharides** from two strains of **Moraxella catarrhalis** serotype C
AUTHOR(S): Edebrink, Per; Jansson, Per-Erik; Mahbubur Rahman, M.; Widmalm, Goeran; Holme, Tord; Rahman, Motiur
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Stockholm, S-106 91, Swed.
SOURCE: Carbohydrate Research (1995), 266(2), 237-61
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The **oligosaccharide** parts from Moraxella (**Branhamella**) **catarrhalis** serotype C **lipooligosaccharides** were isolated by mild acid hydrolysis followed by gel permeation chromatog. Four different **oligosaccharides**, e.g. I, could be identified from strain RS26 and two from strain RS10. The structures of the O-**oligosaccharides** were established by methylation analyses, mass spectrometry, and NMR spectroscopy. It is concluded that the **oligosaccharide** O-**antigens** from RS26 are a mixture of octa-, deca-, and undeca-saccharides, and most likely a heptasaccharide. Strain RS10 contains the deca- and the undeca-saccharide only. Methylation anal. of the intact **lipooligosaccharides** showed that two KDO residues were present, one terminal and one 4,5-substituted residue. It also showed that they consisted of a **lipid A** portion with 6-substituted glucosamine residues.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:34:16 ON 25 AUG 2004)

L20 20 S L18
L21 15 S L20 NOT L10
L22 13 DUP REM L21 (2 DUPLICATES REMOVED)

L22 ANSWER 1 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2004-180545 [17] WPIDS
CROSS REFERENCE: 2004-169460 [16]; 2004-180546 [17]; 2004-180668 [17]; 2004-239150 [22]; 2004-239156 [22]
DOC. NO. CPI: C2004-071430
TITLE: Neisserial bleb preparation derived from a neisserial strain with an L2 **LOS** immunotype or a neisserial strain with an L3 **LOS** immunotype, useful for preparing a vaccine against Neisseria meningitis infection.
DERWENT CLASS: B04 D16
INVENTOR(S): BIEMANS, R; DENOEL, P; FERON, C; GORAJ, K; POOLMAN, J; WEYNANTS, V
PATENT ASSIGNEE(S): (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004014417	A2	20040219	(200417)*	EN	51

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC
VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004014417	A2	WO 2003-EP8568	20030731

PRIORITY APPLN. INFO: GB 2003-5028 20030305; GB
2002-18035 20020802; GB
2002-18036 20020802; GB
2002-18037 20020802; GB
2002-18051 20020802; GB
2002-20197 20020830; GB
2002-20199 20020830; GB
2002-25524 20021101; GB
2002-25531 20021101; GB
2002-30164 20021224; GB
2002-30168 20021224; GB
2002-30170 20021224

AN 2004-180545 [17] WPIDS
CR 2004-169460 [16]; 2004-180546 [17]; 2004-180668 [17]; 2004-239150 [22]; 2004-239156 [22]
AB WO2004014417 A UPAB: 20040331
NOVELTY - A Neisserial bleb preparation derived from a neisserial strain with an L2 **LOS** immunotype or a neisserial strain with an L3 **LOS** immunotype, where the strain is IgtB- or a Neisserial bleb preparation comprising a combination of blebs derived from a neisserial strain with an L2 **LOS** immunotype and a neisserial strain with an L3 **LOS** immunotype, optionally where each strain is IgtB-, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a **LOS** preparation isolated from the Neisserial strains comprising immunotype L2 and/or L3 **LOS**;

(2) an immunogenic composition or vaccine comprising the Neisserial bleb preparation or the **LOS** preparation and an excipient;

(3) a process of manufacturing the Neisserial bleb preparation vaccine;

(4) a process of producing an intra-bleb conjugated bleb preparation from a Gram-negative bacterial strain, where in the outer-membrane of which is integrated an outer-membrane protein conjugated to **LOS**.

ACTIVITY - Antibacterial. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The Neisserial bleb preparation is useful for preparing a vaccine against Neisseria meningitis infection.

Dwg.0/6

L22 ANSWER 2 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-082886 [08] WPIDS
DOC. NO. CPI: C2004-034102

TITLE: New medicament for treating or preventing Neisseria meningitidis infection comprising glycoconjugates and/or **lipooligosaccharides** from commensal bacteria with cross-reactive **antigens** to N. meningitidis.

DERWENT CLASS: B04 D16

INVENTOR(S): BEUTH, J; BLACKWELL, C C; BRAUN, J M; WEIR, D M

PATENT ASSIGNEE(S): (BEUT-I) BEUTH J; (BLAC-I) BLACKWELL C C; (BRAU-I) BRAUN J M; (WEIR-I) WEIR D M

COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004002523	A1	20040108	(200408)*	EN	77
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
EP 1374892	A1	20040102	(200414)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
AU 2003246611	A1	20040119	(200447)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004002523	A1	WO 2003-EP6799	20030627
EP 1374892	A1	EP 2002-14397	20020628
AU 2003246611	A1	AU 2003-246611	20030627

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003246611	A1 Based on	WO 2004002523

PRIORITY APPLN. INFO: US 2002-393741P 20020708; EP 2002-14397 20020628

AN 2004-082886 [08] WPIDS

AB WO2004002523 A UPAB: 20040202

NOVELTY - A medicament for the treatment or prevention of diseases due to infection by Neisseria meningitidis comprising glycoconjugates and/or **lipooligosaccharides** (**LOS**) included in outer membrane vesicles, blebs, **lipid** layers, liposomes and/or killed or commensal bacteria with cross-reactive **antigens** to N. meningitidis of the serogroup A, B, C, H, I, K, L, X, Y, Z, 29E or W135.

DETAILED DESCRIPTION - A medicament for the treatment or prevention of diseases due to infection by Neisseria meningitidis comprising glycoconjugates and/or **lipooligosaccharides** (**LOS**) included in outer membrane vesicles, blebs, **lipid** layers, liposomes and/or killed or commensal bacteria with cross-reactive **antigens** to N. meningitidis of the serogroup A, B, C, H, I, K, L,

X, Y, Z, 29E or W135, or non-capsulated meningococcal strains, and/or antibodies against such glycoconjugates and/or **lipooligosaccharides.**

An INDEPENDENT CLAIM is also included for a diagnostic to assess the susceptibility of patients for diseases due to N. meningitides, comprising glycoconjugates and/or **lipooligosaccharides** from commensal bacteria with cross-reactive **antigens** to N. meningitidis and/or antibodies against such glycoconjugates and/or **lipooligosaccharides.**

ACTIVITY - Antimicrobial.

In three independent experiments, the absorbed and unabsorbed pools were tested for bactericidal activity against 7 isolates of NL. Eighteen meningococcal isolates, including the twelve immunotype reference strains, were tested in the bactericidal assays. The unabsorbed pool killed all the strains tested, the colony forming units (cfu) of each strain was reduced by 80 % that of their respective controls.

MECHANISM OF ACTION - Vaccine.

USE - The methods and compositions of the present invention are useful for the diagnosis, prevention and/or treatment of diseases or conditions due to infection by Neisseria meningitidis.

Dwg.0/12

L22 ANSWER 3 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2004-516882 [49] WPIDS

CROSS REFERENCE: 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]

DOC. NO. CPI: C2004-190698

TITLE: Aerosolizer for intranasal administration of an immunogenic composition comprises Nontypable Haemophilus influenzae or **Moraxella catarrhalis lipooligosaccharide**, useful as a vaccine.

DERWENT CLASS: A96 B04 D16

INVENTOR(S): GU, X

PATENT ASSIGNEE(S): (GUXX-I) GU X

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004126381	A1	20040701	(200449)*		34

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004126381	A1	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423
		Provisional	US 1998-71483P	19980113
		Cont of	WO 1999-US590	19990112
		CIP of	US 2000-610034	20000705
		CIP of	US 2001-789017	20010220
		Provisional	US 2001-288695P	20010503
		Cont of	WO 2001-US32331	20011016
			US 2003-688115	20031017

FILING DETAILS:

Searcher : Shears 571-272-2528

PATENT NO	KIND	PATENT NO
US 2004126381	A1 Div ex	US 6207157
	CIP of	US 6607725
	CIP of	US 6685949

PRIORITY APPLN. INFO: US 2003-688115 20031017; US
1996-16020P 19960423; US
1997-842409 19970423; US
1998-71483P 19980113; WO
1999-US590 19990112; US
2000-610034 20000705; US
2001-789017 20010220; US
2001-288695P 20010503; WO
2001-US32331 20011016

AN 2004-516882 [49] WPIDS
CR 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]
AB US2004126381 A UPAB: 20040802
NOVELTY - An aerosolizer for intranasal administration of an immunogenic composition comprises an immunizing amount of Nontypable Haemophilus influenzae (NTHi) or **Moraxella catarrhalis lipooligosaccharide** (**LOS**) where a primary O-linked fatty acid has been removed to form detoxified **LOS** (**dLOS**) and an immunogenic carrier linked to it, and a mucosal adjuvant or delivery system, is new.

DETAILED DESCRIPTION - In the composition above, the **dLOS** and the immunogenic carrier are optionally covalently linked by a linker.

An INDEPENDENT CLAIM is also included for a method for inducing an immunological response.

ACTIVITY - Immunostimulant; Antibacterial; Respiratory-Gen; Auditory.

MECHANISM OF ACTION - Vaccine.

USE - The aerosolizer for intranasal administration of an immunogenic composition is useful as a vaccine for respiratory diseases caused by NTHi or **M. catarrhalis** infection.

Dwg.0/14

L22 ANSWER 4 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-129162 [12] WPIDS
CROSS REFERENCE: 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2004-516882 [49]
DOC. NO. CPI: C2003-032959
TITLE: Aerosolizer used for treating e.g. otitis media, comprises immunogenic intranasal composition and a mucosal adjuvant or delivery system.
DERWENT CLASS: A96 B04
INVENTOR(S): GU, X
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 4
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002089839	A1	20021114	(200312)*	EN	61
W: AU CA JP US					
AU 2002211782	A1	20021118	(200452)		

Searcher : Shears 571-272-2528

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002089839	A1	WO 2001-US32331	20011016
AU 2002211782	A1	AU 2002-211782	20011016

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002211782	A1 Based on	WO 2002089839

PRIORITY APPLN. INFO: US 2001-288695P 20010503
AN 2003-129162 [12] WPIDS
CR 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2004-516882 [49]
AB WO 200289839 A UPAB: 20040813
NOVELTY - Aerosolizer comprises an immunogenic composition which comprises nontypeable Haemophilus influenza or **Moraxella catarrhalis lipooligosaccharide** (**LOS**) and mucosal adjuvant or delivery system. At least one primary O-linked fatty acid from **LOS** is removed to form detoxified **LOS** (**dLOS**) and an immunogenic carrier covalently linked to it by a linker.

ACTIVITY - Antiinflammatory; Auditory; Antibacterial.

MECHANISM OF ACTION - Vaccine.

Lipooligosaccharide (**LOS**) of (nontypeable Haemophilus influenza) (NTHi) strain 9274 was extracted from cells by hot phenol water and then purified by gel filtration as described in Gu, X.X et. al. 1995 Infect Immun 63:4115-4120. Detoxification of **LOS**, conjugation of **dLOS** to TT and characterization of **dLOS** -TT from strain 9274 were effected as described in Gu, X.X et. al. 1995 Infect Immun 64:4047-4053. The composition of **dLOS**-TT comprised **dLOS** (638 mu g) and TT (901 mu g) in a molar ratio of 35:1. For the enumeration of **LOS**-specific immunoglobulin-producing cells, the numbers of **LOS**-specific IgA-producing cells in nasal associated lymphoid tissue, normal prostate, submandibular glands, spleen, cervical lymph nodes, lung, and small intestine were determined with ELISPOT assay as described in Kodama, S. et. al. 2000 Infect Immun 68:2294-2300.

To examine the effect of the **dLOS**-TT vaccine on NTHi clearance in nasopharynx, the mice immunized with different **antigens** were challenged with the homologous strain 9274. The strain was grown on chocolate agar at 37 deg. C under 5% CO2 for 16 hours and then 3 - 5 clones were transferred to another plate and incubated for 4 hours. A bacterial suspension was prepared to the concentration of 4-6 multiply 106 CFU/ml and the mice were intranasally inoculated with the bacterial suspension (10 mu l). To investigate correlation between antibody levels and bacterial clearance of strain 9274, saliva was collected. To examine the cross-reactivity of antibodies in saliva elicited by the vaccine against heterologous NTHi strains, the homologous NTHi strains 9274 were suspended in PBS to an optical density of 65% transmission. Cholera **toxin** (CT) acted as control. Results of GM antibody ELISA titers for **dLOS**-TT+CT/**dLOS**-CT/CT were 63/6/5.

USE - Used for treating otitis media, other respiratory disease caused by NTHi or **M. catarrhalis** infection and sinusitis in children and in conjugate vaccine and inhibits colonization by NTHi or **Moraxella catarrhalis.**

ADVANTAGE - The aerosolizer induces an immunological response.

Dwg.0/14

L22 ANSWER 5 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-527537 [44] WPIDS
CROSS REFERENCE: 1998-480939 [41]
DOC. NO. NON-CPI: N1999-390731
DOC. NO. CPI: C1999-155020
TITLE: Conjugates used in the treatment of glycolipid mediated states comprising a glycomimetic receptor moiety bound to an active agent and new serine **oligosaccharides**
.
DERWENT CLASS: B02 B04 B05 D16 S03
INVENTOR(S): LINGWOOD, C; MYLVAGANAM, M
PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (HSCR-N) HSC RES DEV LP
COUNTRY COUNT: 81
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9943356	A1	19990902	(199944)*	EN	101
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9889679	A	19990915	(200004)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9943356	A1	WO 1998-CA817	19980826
AU 9889679	A	AU 1998-89679	19980826

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9889679	A Based on	WO 9943356

PRIORITY APPLN. INFO: US 1998-95673P 19980807; US 1998-30095 19980225; WO 1998-CA142 19980226

AN 1999-527537 [44] WPIDS
CR 1998-480939 [41]
AB WO 9943356 A UPAB: 20000124
NOVELTY - Treatment of a glycolipid mediated state comprises administration of a therapeutic compound A-B, wherein A is a glycomimetic receptor moiety and B is an active agent, is new.

DETAILED DESCRIPTION - Treatment of a glycolipid mediated stated

comprises administration of a therapeutic compound A-B wherein A is a glycomimetic receptor moiety and B is an active agent, wherein the glycomimetic receptor moiety includes an **oligosaccharide** moiety coupled to a ceramide **lipid** base, to a serine **lipid** base or to a sphingosine **lipid** base. The active agent is an antibiotic or a carbocyclic compound. INDEPENDENT CLAIMS are also included for the following:

(1) a method of modulating interaction between a pathogen and a glycolipid comprises administering a compound A-B;

(2) a method treating a state characterized by the presence of shiga-like **toxin** in a subject, comprising administering to a subject a compound A-B;

(3) A pharmaceutical composition comprising the structure A-B;

(4) A pharmaceutical composition for treating a glycolipid mediated state in a subject, comprising administering compound A-B, such that a glycolipid mediated state is treated;

(5) A pharmaceutical composition for modulating interaction between a pathogenic microorganism and a glycolipid, comprising compound A-B, such that interaction between a pathogenic microorganism and a glycolipid is modulated.

(6) A packaged therapeutic composition for treating a glycolipid mediated state or for modulating interaction between a pathogenic microorganism and a glycolipid comprises: a container holding a therapeutic compound A-B and instructions for use;

(7) A method for synthesis of serine **oligosaccharides** comprises oxidizing the sphingosine double bond of a glycosphingolipid under basic conditions;

(8) The serine **oligosaccharide** produced in (7) and of the formula: Where, R = acyl, H, phenyl, ketone, methyl ketone, t-butoxide ester; Q = a saccharide moiety;

(9) an assay for determining gp120 binding activity comprises exposing a gp120 binding compound to gp120 so that an intermediate is formed, removing the unbound gp120 from the intermediate, exposing the intermediate to HIV sera and detecting the binding between gp120 of the intermediate and HIV sera and so determining the gp120 binding activity of gp120 binding compound; and

(10) an assay for determining the inhibition between a Shiga-like **toxin** and a glycolipid receptor comprises providing a container coated with a glycolipid receptor, providing an inhibitor, exposing the glycolipid receptor to the inhibitor, providing a Shiga-like **toxin** and analyzing the ability of the **toxin** to bind to the glycolipid receptor and so determining the inhibition of the glycolipid receptor and a Shiga-like **toxin**.

ACTIVITY - Antimicrobial.

MECHANISM OF ACTION - Inhibition or prevention of interaction between the cell membrane surface and the pathogen.

USE - The composition is used to treat glycolipid mediated states associated with pathogenic microorganisms whereby the microorganisms can be bacterial or viral . Microorganisms include Streptococcus pneumoniae, Streptococcus agalactiae (Gp B), **Branhamella catarrhalis** , Chlamydia trachomatis, Chlamydia pneumoniae, Clostridium perfringens, Clostridium difficile, Staphylococcus aureus, Klebsiella pneumoniae, Borrelia burgdorferi, Haemophilus influenza, Haemophilus parainfluenzae, Pseudomonas aeruginosa, Pseudomonas cepacia, Pseudomonas maltophilia, Neisseria gonorrhoeae, Neisseria meningitidis, Helicobacter pylori, Shigella dysenteriae, Shigella flexneri, Pasteurella multocid, Coxiella

burnetti, Mycobacterium tuberculosis, Mycobacterium avium-intracellulare, Salmonella typhymurium, E.coli ATCC 6883, E.coli HB101/Dh5a, VTEC, Influenza A, B and C viruses or HIV. The compositions are especially useful for treating conditions caused by Shiga-like **toxins** wherein the Shiga like **toxin** is SLT1, SLTII , SLTIII or a cytotoxin similar in structure and function to a shiga-like **toxin**

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Dwg.0/24

L22 ANSWER 6 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-070180 [06] WPIDS
DOC. NO. CPI: C1999-020714
TITLE: New laft mutants of gram-negative pathogenic bacteria - produce **LOS** having reduced toxicity, but retaining antigenicity, useful for immunisation against gram negative bacteria.
DERWENT CLASS: B04 D16
INVENTOR(S): APICELLA, M A; GIBSON, B W; NICHOLS, W A
PATENT ASSIGNEE(S): (APIC-I) APICELLA M A; (GIBS-I) GIBSON B W; (NICH-I) NICHOLS W A; (REGC) UNIV CALIFORNIA; (IOWA) UNIV IOWA RES FOUND
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9853851	A1	19981203	(199906)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9877010	A	19981230	(199918)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9853851	A1	WO 1998-US10881	19980528
AU 9877010	A	AU 1998-77010	19980528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9877010	A	Based on	WO 9853851

PRIORITY APPLN. INFO: US 1997-47791P 19970528
AN 1999-070180 [06] WPIDS
AB WO 9853851 A UPAB: 19990316
A bacterium (I), particularly a Gram negative bacterium, that has its **Lipid** A fatty transferase (LAft) gene mutated to remove transferase activity (designated a laft mutant), is new. Also claimed are: (1) an endotoxin isolated from a laft mutant bacterium (2) a method of preparing mutant endotoxin, by isolating it from (I), where the mutated

endotoxin has substantially reduced toxicity relative to that from the corresponding wild-type bacterium (3) a vaccine comprising: (a) a laft mutant bacterium, particularly where the bacterium is live and inactivated; (b) a physiological carrier suitable for mucosal administration.

USE - (I) is used to immunise an individual, particularly a human against a live gram negative bacterial pathogen (claimed). Gram negative pathogens including Neisseria meningitides, N. gonorrhoeae, Haemophilus species including H. influenzae and H. ducreyi, and **Moraxella catarrhalis** are particular targets for the vaccine, especially H. influenzae. Laft mutants can be engineered to express heterologous **antigens** of other microbial pathogens at the surface of the mutated bacteria for use as a multivalent vaccine. Isolated endotoxin from laft mutants, either alone, or conjugated to a carrier protein, may be used to generate **lipooligosaccharides** (**LOS**)-specific antibodies for passive immunisation and for diagnostic assays to detect gram-negative pathogens in clinical specimens (disclosed).

Dwg.0/1

L22 ANSWER 7 OF 13 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-480939 [41] WPIDS
CROSS REFERENCE: 1999-527537 [43]
DOC. NO. CPI: C1998-145518
TITLE: Treating glyco-**lipid** mediated state - comprises administration of compound comprising glyco-**lipid** receptor group and active agent.
DERWENT CLASS: B02
INVENTOR(S): LINGWOOD, C A
PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9837915	A1	19980903	(199841)*	EN	59

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9860845	A	19980918	(199908)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9837915	A1	WO 1998-CA142	19980226
AU 9860845	A	AU 1998-60845	19980226

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9860845	A	Based on	WO 9837915

Searcher : Shears 571-272-2528

PRIORITY APPLN. INFO: US 1997-39160P 19970226
AN 1998-480939 [41] WPIDS
CR 1999-527537 [43]
AB WO 9837915 A UPAB: 19991026
Treating a glycolipid mediated state comprises administration of a compound of formula A-B (I). A = glycolipid receptor group and B = active agent. Also claimed are: (1) a composition comprising (I) and a carrier and (2) a packaged therapeutic composition comprising a container holding (I) and instructions for using the composition.

The glycolipid receptor group preferably includes an **oligosaccharide** group coupled to a ceramide **lipid** base. The active agent is an antibiotic, preferably a penicillin, cepham or a cephalosporin or the active agent is a carbocyclic compound, preferably an adamantyl or acridine derivative.

USE - The method is used for treating glycolipid mediated state associated with a pathogenic microorganism, particularly a bacteria comprising Streptococcus pneumoniae, Streptococcus agalactiae (Gp.B), **Branhamella catarrhalis**, Chlamydia trachomatis, Chlamydia pneumoniae, Clostridium perfringens, Clostridium difficile, Staphylococcus aureus, Klebsiella pneumoniae, Borrelia burgdorferi, Haemophilus influenzae, Haemophilus parainfluenzae, Pseudomonas aeruginosa, Pseudomonas cepacia, Pseudomonas maltophilia, Neisseria gonorrhoeae, Neisseria meningitidis, Helicobacter pylori, Shigella dysenteriae, Shigella flexneri, Pasturella, multocida, Coxiella burnetti, Mycobacterium tuberculosis, Mycobacterium avium-intracellulare, Salmonella typhymurium, Escherichia coli ATCC 6883 and Escherichia coli HB101/DH5a or the bacteria VTEC. The method is also used for treating a state characterised by a shiga-like **toxin**, preferably verotoxin, a SLTI, a SLTII, a SLTIII or any cytotoxin similar in both structure and function to Shiga **toxin**. The dosage is 0.0001-200 (especially 0.2-140) mg/kg/day intravenously or subcutaneously.

ADVANTAGE - None given.

Dwg.0/9

L22 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:831159 SCISEARCH
THE GENUINE ARTICLE: VR778
TITLE: MONOCLONAL-ANTIBODIES AGAINST HAEMOPHILUS-INFLUENZAE LIPOPOLYSACCHARIDES - CLONE MAHI-4 BINDING TO A PENTASACCHARIDE CONTAINING TERMINAL BETA-GAL RESIDUES AND CLONE MAHI-10 RECOGNIZING TERMINAL PHOSPHORYLATED SACCHARIDE RESIDUES
AUTHOR: BORRELLI S; JANSSON P E (Reprint); LINDBERG A A
CORPORATE SOURCE: KAROLINSKA INST, HUDDINGE HOSP, NOVUM, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN (Reprint); KAROLINSKA INST, HUDDINGE HOSP, NOVUM, CLIN RES CTR, S-14186 HUDDINGE, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: MICROBIAL PATHOGENESIS, (NOV 1996) Vol. 21, No. 5, pp. 307-318.
ISSN: 0882-4010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 25

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mouse monoclonal antibodies MAHI 4 and MAHI 10 reactive with Haemophilus influenzae lipopolysaccharide (LPS), were generated by fusing mouse myeloma cells with spleen cells of mice immunized with H. influenzae strain RM.7004-XP-1. The antibody MAHI 4 reacted in whole-cell enzyme immunoassay (EIA) and colony-dot-immunoblotting with 20 of 123 H. influenzae strains and to a few other human Haemophilus spp. and Neisseria spp., but not to any Bordetella pertussis, B. parapertussis, Aeromonas spp. or **Moraxella catarrhalis** strains tested. This suggests a specific epitope accessible to recognition in just a few strains. This conclusion was supported by the data on binding of MAHI 4 to only three of 18 H. influenzae LPSs tested, but not td any Haemophilus ducreyi or enterobacterial LPSs. The antibody MAHI 10 bound to 80 of 123 strains of H. influenzae and to a few strains of Neisseria spp. and **M. catarrhalis** as evaluated by EIA and colony-dot-immunoblotting, which suggests an epitope accessible to recognition in 65% of the H. influenzae strains tested. The antibody MAHI 10 reacted with 10 of 18 H. influenzae LPSs as determined by EIA. By using polysaccharides, obtained after both mild acidic hydrolysis, strong alkali treatment, and dephosphorylation, as inhibitors of the antibodies binding to N. influenzae LPS **antigens** it was shown that phosphate groups were essential for the binding of MAHI 10 to LPS but they did not affect antigenic recognition by MAHI 4. None of the monoclonal antibodies bound to isolated **lipid A**, but the aggregation caused by the fatty acids of **lipid A** was essential for optimum epitope recognition. Enzymatic treatment of homologous LPSs with galactose-oxidase led to products which were between 20 to 30 times less effective as inhibitors of the binding of the MAHI 4 than the native LPSs. Taken together the results indicate that MAHI 4 has the following pentasaccharide as the epitope Gal beta 1-->2Hep alpha 1-->2Hep alpha 1-->3Hep alpha 1-->Kdo(P). These results emphasize the importance of the terminal beta-Gal residue in the definition of the MAHI 4 specificity, and of the terminal phosphorlylated saccharide residues of some of the Haemophilus LPSs for the MAHI 10 specificity. (C) 1996 Academic Press Limited

L22 ANSWER 9 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:23710 SCISEARCH
THE GENUINE ARTICLE: VZ169
TITLE: The structures of **oligosaccharides** isolated from the lipopolysaccharide of **Moraxella catarrhalis** serotype B, strain CCUG 3292
AUTHOR: Edebrink P; Jansson P E (Reprint); Widmalm G; Holme T; Rahman M
CORPORATE SOURCE: HUDDINGE HOSP, KAROLINSKA INST, NOVUM, CLIN RES CTR, ANALYT UNIT, S-14186 HUDDINGE, SWEDEN (Reprint); HUDDINGE HOSP, KAROLINSKA INST, NOVUM, CLIN RES CTR, ANALYT UNIT, S-14186 HUDDINGE, SWEDEN; UNIV STOCKHOLM, ARRHENIUS LAB, DEPT ORGAN CHEM, S-10691 STOCKHOLM, SWEDEN; KAROLINSKA INST, DIV BACTERIOL, CTR MICROBIOL & TUMOR BIOL, S-17177 STOCKHOLM, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: CARBOHYDRATE RESEARCH, (13 DEC 1996) Vol. 295, pp. 127-146

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

Searcher : Shears 571-272-2528

ISSN: 0008-6215.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The **oligosaccharides** from the lipopolysaccharides of **Moraxella catarrhalis** serotype B, strain CCUG 3292, were isolated after mild acid hydrolysis and separated by high-performance anion-exchange chromatography. The structures of the **oligosaccharides** were established by fast atom bombardment mass spectrometry and nuclear magnetic resonance spectroscopy. It is concluded that the **oligosaccharides** comprise a mixture of mainly a nona- and a deca-saccharide.
[GRAPHICS]
Smaller amounts of undecasaccharides and of truncated forms. namely, hexa-, hepta-, and octa-saccharides, were also detected. (C) 1996 Elsevier Science Ltd.

L22 ANSWER 10 OF 13 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 95211773 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7535189
TITLE: Structural studies of the O-**antigen** **oligosaccharides** from two strains of **Moraxella catarrhalis** serotype C.
AUTHOR: Edebrink P; Jansson P E; Rahman M M; Widmalm G; Holme T; Rahman M
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Sweden.
SOURCE: Carbohydrate research, (1995 Jan 17) 266 (2) 237-61. Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19960129
Entered Medline: 19950504

AB The **oligosaccharide** parts from Moraxella (**Branhamella**) **catarrhalis** serotype C **lipooligosaccharides** were isolated by mild acid hydrolysis followed by gel permeation chromatography. Four different **oligosaccharides** could be identified from strain RS26 and two from strain RS10. The structures of the O-**oligosaccharides** were established by methylation analyses, mass spectrometry, and NMR spectroscopy. It is concluded that the **oligosaccharide** O-**antigens** from RS26 are a mixture of octa-, deca-, and undeca-saccharides, and most likely a heptasaccharide. Strain RS10 contains the deca- and the undeca-saccharide only. The structures for the **oligosaccharides** are shown below. [formula: see text] **OS**(7) [formula: see text] **OS**(8) [formula: see text] **OS**(10) [formula: see text] **OS**(11) Methylation analysis of the intact **lipooligosaccharides** showed that two Kdo residues were present, one terminal and one 4,5-substituted residue. It also showed that they consisted of a **lipid** **A** portion with 6-substituted glucosamine residues.

L22 ANSWER 11 OF 13 MEDLINE on STN
ACCESSION NUMBER: 94282800 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7516823
TITLE: Structural studies of the O-polysaccharide from the lipopolysaccharide of Moraxella (**Branhamella**) **catarrhalis** serotype A (strain ATCC 25238).
AUTHOR: Edebrink P; Jansson P E; Rahman M M; Widmalm G; Holme T; Rahman M; Weintraub A
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Sweden.
SOURCE: Carbohydrate research, (1994 May 5) 257 (2) 269-84. Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940810
Last Updated on STN: 19960129
Entered Medline: 19940726

AB The polysaccharide of the Moraxella (**Branhamella**) **catarrhalis** serotype A lipopolysaccharide was prepared by mild acid hydrolysis followed by gel permeation chromatography. The structure was established by methylation analysis, mass spectrometry, and NMR spectroscopy. It is concluded that the O-antigenic polysaccharide has the following structure. [formula see text] Methylation analysis of the intact lipopolysaccharide showed that the **lipid A** portion consisted of 6-substituted glucosamine residues. Methylation followed by methanolysis showed that two Kdo residues were present, one terminal and one 4,5-substituted residue. A terminal Kdo thus substitutes the branch-point Kdo in the 4-position.

L22 ANSWER 12 OF 13 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94196523 EMBASE
DOCUMENT NUMBER: 1994196523
TITLE: Isolation and characterization of lipopolysaccharides, **lipooligosaccharides**, and **lipid A**
AUTHOR: Apicella M.A.; Griffiss J.M.; Schneider H.
CORPORATE SOURCE: Department of Microbiology, Iowa University College of Medicine,Iowa City, IA 52242, United States
SOURCE: Methods in Enzymology, (1994) 235/- (242-252). ISSN: 0076-6879 CODEN: MENZAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

L22 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:143709 SCISEARCH
THE GENUINE ARTICLE: MW919
TITLE: CHARACTERIZATION OF THE LIPOPOLYSACCHARIDE OF **MORAXELLA-CATARRHALIS** STRUCTURAL-ANALYSIS OF THE **LIPID-A**

Searcher : Shears 571-272-2528

FROM **M CATARRHALIS** SEROTYPE-A
LIPOPOLYSACCHARIDE

AUTHOR: MASOUD H; FERRY M B; RICHARDS J C (Reprint)
CORPORATE SOURCE: NATL RES COUNCIL CANADA, INST BIOL SCI, OTTAWA K1A 0R6, ON, CANADA (Reprint); NATL RES COUNCIL CANADA, INST BIOL SCI, OTTAWA K1A 0R6, ON, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (15 FEB 1994) Vol. 220, No. 1, pp. 209-216.
ISSN: 0014-2956.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The lipopolysaccharide of **Moraxella catarrhalis** serotype A (ATCC 25238) was found to consist of a short-chain **oligosaccharide** attached to a **lipid A** moiety. Composition and NMR analyses showed the **oligosaccharide** component in O-deacylated LPS to be composed of D-glucose, D-galactose, 2-acetamido-2-deoxy-D-glucose and 3-deoxy-D-manno-octulosonic acid in the molar ratio of 5:2:1:2. In addition, the **lipid A** region contained phosphate, D-glucosamine, ethanolamine, 3-hydroxydodecanoic acid, dodecanoic acid and decanoic acid. The **lipid A** was examined in detail by high-field NMR spectroscopy and mass spectrometry. It was found to consist of a beta-1,6-D-glucosamine disaccharide backbone esterified at C4' by a phosphomonoester and glycosidically at C1 by diphosphoethanolamine or phosphomonoester. The amide group of the reducing and nonreducing glucosamine residues were acylated by 3-dodecanoyloxydodecanoic acid and 3-decanoyloxydodecanoic acid, respectively. The hydroxyl group at C3 and C3' were acylated by 3-decanoyloxydodecanoic acid and 3-hydroxydodecanoic acid respectively, while the hydroxyl groups at C4 and C6' were unsubstituted.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:38:39 ON 25 AUG 2004)

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L23        5996 S "GU X"?/AU
L24        6548 S "ROBBINS J"?/AU
L25          32 S L23 AND L24
L26          51 S (L23 OR L24) AND L6
L27          75 S L25 OR L26
L28          28 DUP REM L27 (47 DUPLICATES REMOVED)
L29          37 S (L23 OR L24) AND L12
L30          61 S L25 OR L29
L31          23 DUP REM L30 (38 DUPLICATES REMOVED)
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- Author (s)

L31 ANSWER 1 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:130022 BIOSIS
DOCUMENT NUMBER: PREV200400130700
TITLE: **Lipooligosaccharide** based vaccine for prevention of moraxella (**branhamella**)**catarrhalis** infections in humans.
AUTHOR(S): **Gu, Xin-Xing** [Inventor, Reprint Author]; **Robbins, John B.** [Inventor]
CORPORATE SOURCE: ASSIGNEE: The United States of America as represented by

the Department of Health & Human Services
PATENT INFORMATION: US 6685949 February 03, 2004
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb 3 2004) Vol. 1279, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

AB A conjugate vaccine for Moraxella (**Branhamella**) **catarrhalis** comprising isolated **lipooligosaccharide** from which esterified fatty acids have been removed, to produce a detoxified **lipooligosaccharide** (**dLOS**), or from which lipid A has been removed, to produce a detoxified **oligosaccharide** (**OS**), which is linked to an immunogenic carrier. The vaccine is useful for preventing otitis media and respiratory infections caused by **M. catarrhalis** in mammals, including humans.

L31 ANSWER 2 OF 23 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-516882 [49] WPIDS
CROSS REFERENCE: 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]
DOC. NO. CPI: C2004-190698
TITLE: Aerosolizer for intranasal administration of an immunogenic composition comprises Nontypable Haemophilus influenzae or **Moraxella catarrhalis** **lipooligosaccharide**, useful as a vaccine.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): **GU, X**
PATENT ASSIGNEE(S): (GUXX-I) GU X
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004126381	A1	20040701	(200449)*		34

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004126381	A1	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423
		Provisional	US 1998-71483P	19980113
		Cont of	WO 1999-US590	19990112
		CIP of	US 2000-610034	20000705
		CIP of	US 2001-789017	20010220
		Provisional	US 2001-288695P	20010503
		Cont of	WO 2001-US32331	20011016
			US 2003-688115	20031017

FILING DETAILS:

PATENT NO	KIND	PATENT NO

Searcher : Shears 571-272-2528

US 2004126381 A1 Div ex US 6207157
CIP of US 6607725
CIP of US 6685949

PRIORITY APPLN. INFO: US 2003-688115 20031017; US
1996-16020P 19960423; US
1997-842409 19970423; US
1998-71483P 19980113; WO
1999-US590 19990112; US
2000-610034 20000705; US
2001-789017 20010220; US
2001-288695P 20010503; WO
2001-US32331 20011016

AN 2004-516882 [49] WPIDS
CR 1999-444322 [37]; 2001-272747 [28]; 2002-163687 [21]; 2003-129162 [12]
AB US2004126381 A UPAB: 20040802
NOVELTY - An aerosolizer for intranasal administration of an immunogenic composition comprises an immunizing amount of Nontypable Haemophilus influenzae (NTHi) or **Moraxella catarrhalis lipooligosaccharide** (**LOS**) where a primary O-linked fatty acid has been removed to form detoxified **LOS** (**dLOS**) and an immunogenic carrier linked to it, and a mucosal adjuvant or delivery system, is new.
DETAILED DESCRIPTION - In the composition above, the **dLOS** and the immunogenic carrier are optionally covalently linked by a linker.
An INDEPENDENT CLAIM is also included for a method for inducing an immunological response.
ACTIVITY - Immunostimulant; Antibacterial; Respiratory-Gen; Auditory.
MECHANISM OF ACTION - Vaccine.
USE - The aerosolizer for intranasal administration of an immunogenic composition is useful as a vaccine for respiratory diseases caused by NTHi or **M. catarrhalis** infection.
Dwg.0/14

L31 ANSWER 3 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2004294285 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15193241
TITLE: Detection of **LOS**-specific antibody-secreting cells by ELISPOT assay.
AUTHOR: Jiao Xin-an; Hirano Takashi; **Gu Xin-xing**
CORPORATE SOURCE: College of Bioscience and Biotechnology, Yangzhou University, Yangzhou 225009, China.. xajiao@yahoo.com
SOURCE: Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi, (2004 May) 20 (3) 366-9.
Journal code: 101139110. ISSN: 1007-8738.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040615
Last Updated on STN: 20040818
AB AIM: To detect dynamically the response of specific antibody-secreting cells elicited by a detoxified-**lipooligosaccharide** -cross-reactive mutant (**dLOS**-CRM) of diphtheria toxin conjugate vaccine for **Moraxella catarrhalis** (M.cat). METHODS: BALB/c mice were intranasally immunized with **dLOS**-CRM conjugate

vaccine. The specific antibody-secreting cells responding to **LOS** of M. cat in different inductive and effective sites, including nasally associated lymphoid tissues (NALT), spleen, cervical lymph nodes (CLN), nasal passages (NP), lungs and Peyer's patches (PP) were detected by an enzyme-linked immunospot assay (ELISPOT). The levels of **LOS** -specific antibodies IgA, IgG and IgM in serum, nasal flush fluid, alveolar douche fluid, saliva and fecal extract were also detected by ELISA. RESULTS: Intranasal immunization with **dLOS**-CRM plus cholera toxin induced a significantly dose-dependent enhancement of immune response. **LOS**-specific antibody (IgA, IgG or IgM)-secreting cells were found in NALT, spleens, CLN, NP, lungs and PP with most **LOS**-specific IgA antibody-secreting cells located in nasal passages, and next, NALT and lungs. It was correlated well with the level of **LOS**-specific IgA, IgG or IgM antibody titers in nasal flush fluid, alveolar douche fluid, saliva, serum and fecal extract. CONCLUSION: **dLOS**-CRM can induce specific mucosal and systemic humoral immune response through intranasal immunization. ELISPOT assay is quick, sensitive, specific, and would be a very useful tool to analyze dynamically the mechanism of single antibody-secreting cell response.

L31 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:407493 CAPLUS
DOCUMENT NUMBER: 141:138789
TITLE: Exploration of **Moraxella catarrhalis** outer membrane proteins, CD and UspA, as new carriers for **lipooligosaccharide**-based conjugates
AUTHOR(S): Hu, Wei-Gang; Berry, Julie; Chen, Jing; **Gu, Xin-Xing**
CORPORATE SOURCE: Vaccine Research Section, National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA
SOURCE: FEMS Immunology and Medical Microbiology (2004), 41(2), 109-115
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Moraxella catarrhalis** outer membrane proteins, CD and ubiquitous surface protein A (UspA), were used as carriers for **M . catarrhalis** detoxified **lipooligosaccharide** (**dLOS**)-based conjugates. This study was designed to investigate the feasibility of CD and UspA as protein carriers for **dLOS** -based conjugates and their possible synergic effects on protection from both anti-**LOS** and anti-CD or anti-UspA antibody responses. Female Balb/c mice were immunized s.c. three times with **dLOS**-CD or **dLOS**-UspA conjugate in Ribi adjuvant. Antisera elicited by the conjugates showed high titers of specific anti-**LOS** antibodies with complement-dependent bactericidal activity towards **M. catarrhalis** strain 25238. In a mouse aerosol challenge model, mice immunized with both conjugates showed a significant enhancement of the clearance of strain 25238 from lungs as compared with the control mice. Although both conjugates elicited reduced (relative to unconjugated CD or UspA) but significant levels of anti-CD or UspA antibodies, they did not show synergetic effects with anti-**LOS** antibodies on the bactericidal activity or the pulmonary bacterial clearance. Nevertheless, CD and UspA are safe and effective new carriers

for **dLOS**-based or other potential carbohydrate-based conjugate vaccines to help thymus-independent carbohydrate antigens for production of anti-carbohydrate antibodies against target pathogens.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:422205 BIOSIS
DOCUMENT NUMBER: PREV200300422205
TITLE: Conjugate vaccine for nontypeable Haemophilus influenzae.
AUTHOR(S): **Gu, Xin-Xing** [Inventor, Reprint Author]; Tsai, Chao-Ming [Inventor]; Lim, David J. [Inventor]; **Robbins, John B.** [Inventor]
CORPORATE SOURCE: College Park, MD, USA
ASSIGNEE: The United States of America as represented by the Department of Health and Human Services
PATENT INFORMATION: US 6607725 August 19, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug 19 2003) Vol. 1273, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 2003
Last Updated on STN: 10 Sep 2003

AB A conjugate vaccine for Nontypeable Haemophilus influenzae comprising lipooligosaccharide from which esterified fatty acids have been removed conjugated to an immunogenic carrier. The vaccine is useful for prevention of otitis media and respiratory infections in mammals.

L31 ANSWER 6 OF 23 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003156563 EMBASE
TITLE: Phase I study of a lipooligosaccharide-based conjugate vaccine against nontypeable Haemophilus influenzae.
AUTHOR: **Gu X.-X.**; Rudy S.F.; Chu C.; McCullagh L.; Kim H.N.; Chen J.; Li J.; **Robbins J.B.**; Van Waes C.; Battey J.F.
CORPORATE SOURCE: X.-X. Gu, Natl. Inst. Deafness/Commun. Disord., 5 Research Court, Rockville, MD 20850, United States. guxx@nidcd.nih.gov
SOURCE: Vaccine, (16 May 2003) 21/17-18 (2116-2123). ~~Refs: 48~~
ISSN: 0264-410X CODEN: VACCDE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Nontypeable Haemophilus influenzae (NTHi) accounts for about one-third of purulent otitis media (OM) in children and is a common cause of pulmonary infection in adults with decreased resistance. Based upon sero-epidemiological data in humans and immunochemical data in laboratory

animals, a lipooligosaccharide (LOS)-tetanus toxoid (TT) conjugate was prepared and evaluated for its safety and immunogenicity in a Phase I study of 40 healthy adults. The conjugate was injected intramuscularly into all volunteers: 28 of them received a second injection 14 weeks later. Local and systemic reactions were monitored and sera, taken before and 2, 6, 14, 16, and 38 weeks after injection, were assayed for IgG, IgA, and IgM antibodies to the LOS by ELISA and for bactericidal activity. The results indicate that there were no significant local or systemic reactions after either injection. All volunteers had pre-existing IgG anti-LOS. The geometric mean (GM) level rose from 14 to 40 at 2 weeks, remained at 35 at 6 weeks (40 or 35 versus 14, $P<0.01$) and dropped to 27 at 14 weeks after the first injection. There was also a rise 2 weeks after the second injection (27 versus 37, $P<0.05$). A total of 52.5% of subjects showed serum-conversion (greater than four-fold increase) after one and two injections. At 38 weeks, the GM IgG anti-LOS was still higher than before initial injection (20 versus 14, $P<0.05$). A similar pattern of reactivity was observed for IgA and IgM anti-LOS. Similar to that observed in mice, but not in rabbits, the conjugate-induced antibodies did not yield significant bactericidal activity in vitro. The LOS-TT conjugate is well tolerant in adults and a Phase II evaluation of the conjugate in children is planned.

L31 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:311602 CAPLUS
DOCUMENT NUMBER: 139:148101
TITLE: Phase I study of a lipooligosaccharide-based conjugate vaccine against nontypeable Haemophilus influenzae
AUTHOR(S): **Gu, Xin-Xing**; Rudy, Susan F.; Chu, Chiayung; McCullagh, Linda; Kim, Hung N.; Chen, Jing; Li, Jianping; **Robbins, John B.**; Van Waes, Carter; Battey, James F.
CORPORATE SOURCE: National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA
SOURCE: Vaccine (2003), 21(17-18), 2107-2114
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Non-typeable Haemophilus influenzae (NTHi) accounts for about one-third of purulent otitis media (OM) in children and is a common cause of pulmonary infection in adults with decreased resistance. Based upon sero-epidemiol. data in humans and immunochem. data in laboratory animals, a lipooligosaccharide (LOS)-tetanus toxoid (TT) conjugate was prepared and evaluated for its safety and immunogenicity in a Phase I study of 40 healthy adults. The conjugate was injected i.m. into all volunteers: 28 of them received a second injection 14 wk later. Local and systemic reactions were monitored and sera, taken before and 2, 6, 14, 16, and 38 wk after injection, were assayed for IgG, IgA, and IgM antibodies to the LOS by ELISA and for bactericidal activity. The results indicate that there were no significant local or systemic reactions after either injection. All volunteers had pre-existing IgG anti-LOS. The geometric mean (GM) level rose from 14 to 40 at 2 wk, remained at 35 at 6 wk (40 or 35 vs. 14) and dropped to 27 at 14 wk after the first injection. There was also a rise 2 wk after the second injection (27 vs. 37). A total of 52.5% of subjects showed serum-conversion (greater than four-fold increase) after one and

two injections. At 38 wk, the GM IgG anti-LOS was still higher than before initial injection (20 vs. 14). A similar pattern of reactivity was observed for IgA and IgM anti-LOS. Similar to that observed in mice, but not in rabbits, the conjugate-induced antibodies did not yield significant bactericidal activity in vitro. The LOS-TT conjugate is well tolerant in adults and a Phase II evaluation of the conjugate in children is planned.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:868765 CAPLUS
DOCUMENT NUMBER: 137:336726
TITLE: Intranasal immunization with detoxified **lipooligosaccharide** from nontypeable Haemophilus influenzae or **Moraxella catarrhalis**
INVENTOR(S): **Gu, Xin-Xing**
PATENT ASSIGNEE(S): United States, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002089839	A1	20021114	WO 2001-US32331		20011016
W: AU, CA, JP, US					
US 2004126381	A1	20040701	US 2003-688115		20031017
PRIORITY APPLN. INFO.:			US 2001-288695P	P	20010503
			US 1996-16020P	P	19960423
			US 1997-842409	A3	19970423
			US 1998-71483P	P	19980113
			WO 1999-US590	A1	19990112
			US 2000-610034	A2	20000705
			US 2001-789017	A2	20010220
			WO 2001-US32331	A1	20011016

AB The invention relates to intranasal immunization with detoxified **lipooligosaccharide** from nontypeable Haemophilus influenzae or **Moraxella catarrhalis**. The detoxified **lipooligosaccharide** can be conjugated to an immunogenic carrier, such as tetanus toxoid or diphtheria toxin. The detoxified **lipooligosaccharide** is administered intranasally with an adjuvant or delivery system.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 9 OF 23 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-163687 [21] WPIDS
CROSS REFERENCE: 1999-444322 [37]; 2001-272747 [28]; 2003-129162 [12]; 2004-516882 [49]
DOC. NO. CPI: C2002-050468
TITLE: Conjugate vaccine useful for the treatment of nontypeable

Haemophilus influenzae, a causative agent for acute otitis media comprises a lipooligosaccharide from which esterified fatty acids have been removed and an immunogenic carrier.

DERWENT CLASS: B04

INVENTOR(S): **GU, X**; LIM, D J; **ROBBINS, J B**; TSAI, C

PATENT ASSIGNEE(S): (GUXX-I) GU X; (LIMD-I) LIM D J; (ROBB-I) ROBBINS J B; (TSAI-I) TSAI C; (USSH) US DEPT HEALTH & HUMAN SERVICES

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002001589	A1	20020103	(200221)*		10
US 6607725	B2	20030819	(200356)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002001589	A1	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423
			US 2001-789017	20010220
US 6607725	B2	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423
			US 2001-789017	20010220

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2002001589	A1	Div ex	US 6207157
US 6607725	B2	Div ex	US 6207157

PRIORITY APPLN. INFO: US 1996-16020P 19960423; US 1997-842409 19970423; US 2001-789017 20010220

AN 2002-163687 [21] WPIDS

CR 1999-444322 [37]; 2001-272747 [28]; 2003-129162 [12]; 2004-516882 [49]

AB US2002001589 A UPAB: 20040802

NOVELTY - A conjugate vaccine comprises a lipooligosaccharide (DLOS) from which esterified fatty acids have been removed and an immunogenic carrier covalently linked to it.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) isolated nontypeable Haemophilus influenzae (NTHi) lipooligosaccharide detoxified by the removal of ester-linked fatty acids;

(2) a method of detoxifying lipooligosaccharide from NTHi involving the removal of ester-linked fatty acids;

(3) a pharmaceutical composition comprising the vaccine conjugate in a carrier; and

(4) preparing the conjugate vaccine against NTHi involving removing ester-linked fatty acids from NTHi lipooligosaccharide to produce (dLOS).

ACTIVITY - Auditory; Virucide; Immunostimulant.

MECHANISM OF ACTION - Vaccine.

USE - For the preparation of a conjugate vaccine for the treatment of Haemophilus influenzae causing otitis media in a mammal (claimed).

ADVANTAGE - The vaccine is detoxified by removing esterified fatty acids and elicits improved bactericidal response.

Dwg.0/5

L31 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2002:815711 CAPLUS
DOCUMENT NUMBER: 137:293239
TITLE: Specific immune responses and enhancement of murine pulmonary clearance of **Moraxella catarrhalis** by intranasal immunization with a detoxified **lipooligosaccharide** conjugate vaccine
AUTHOR(S): Jiao, Xinan; Hirano, Takashi; Hou, Yingchun; **Gu, Xin-Xing**
CORPORATE SOURCE: National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, 20850, USA
SOURCE: Infection and Immunity (2002), 70(11), 5982-5989
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Moraxella catarrhalis** is an important human mucosal pathogen. This study investigated the effect of intranasal immunization with a detoxified-**lipooligosaccharide**-cross-reactive mutant of diphtheria toxin (**dLOS**-CRM) vaccine candidate on pulmonary clearance following an aerosol challenge of mice with **M. catarrhalis**. Intranasal immunization with **dLOS**-CRM plus cholera toxin induced a significantly dose-dependent increase of IgA and IgG in the nasal wash, lung lavage fluid, saliva, and fecal extract In addition, serum IgG, IgM, and IgA against **LOS** of **M. catarrhalis** were detected. **LOS**-specific antibody-forming cells were found in the nasal passages, spleens, nasally associated lymphoid tissues, cervical lymph nodes, lungs, and Peyer's patches using an enzyme-linked immunospot assay. The **dLOS**-CRM vaccine induced a significant bacterial clearance (70 to 90%) of both homologous and heterologous strains in the lungs compared to that observed in the controls ($P < 0.01$). Intriguingly, intranasal immunization with **dLOS**-CRM showed a higher level of bacterial clearance compared with s.c. injections with **dLOS**-CRM. These data indicate that **dLOS**-CRM induces specific mucosal and systemic immunity through intranasal immunization and also provides effective bacterial clearance. On the basis of these results, we believe that **dLOS**-CRM should undergo continued testing to determine whether it would induce protective immune response in humans.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:585448 BIOSIS
DOCUMENT NUMBER: PREV200200585448
TITLE: Nasopharyngeal clearance of **Moraxella catarrhalis** in a mouse model.

AUTHOR(S): Jiao, X. [Reprint author]; Hirano, T. [Reprint author]; Hou, Y. [Reprint author]; **Gu, X.** [Reprint author]
CORPORATE SOURCE: NIH, Rockville, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 172. print. Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology. ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

AB **Moraxella catarrhalis** is a significant cause of otitis media in children as well as lower respiratory tract infections in the elderly. One of the prerequisites for infections caused by **M. catarrhalis** is bacterial colonization in the nasopharynx. Little is known about the interaction between **M. catarrhalis** and nasopharynx, and the roles of immune responses in affecting this process, since there is no animal model available. In this study, a simple, reproducible, and non-invasive mouse nasopharyngeal clearance model for **M. catarrhalis** via an aerosol challenge was established. All of four tested strains could be inoculated into mouse nasopharynx at more than 10 to 4 colony-forming units (CFU) with a challenge concentration of 5X10 to 8-1X10 to 9 CFU/ml in a nebulizer. The number of bacteria retained at 6 h postchallenge was more than 10 to 3 CFU/mouse, while at 24 h postchallenge, approximately 10 to 2 CFU in the nasopharynx. The bacteria in nasopharynx were cleared out within 72 h, but in the lungs it was less than 48 h. The number of bacteria inoculated in the nasopharynx could be adjusted on the bacterial challenge concentration, the exposure time, and the negative pressure. Active immunization with inactivated whole cells of **M. catarrhalis** or detoxified **lipooligosaccharide**-protein conjugate vaccines significantly enhanced nasopharyngeal clearance of homologous strain in this model. These data indicate that this model will be useful for evaluating the efficacy of vaccines against diseases caused by **M. catarrhalis** and studying the mechanisms of immunity against **M. catarrhalis**.

L31 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:224354 CAPLUS
DOCUMENT NUMBER: 134:251197
TITLE: Conjugate vaccine for nontypeable Haemophilus influenzae
INVENTOR(S): **Gu, Xin-xing**; Tsai, Chao-ming; Lim, David J.; **Robbins, John B.**
PATENT ASSIGNEE(S): The United States of America as Represented by the Department of Health and Human Services, USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6207157	B1	20010327	US 1997-842409		19970423
US 2002001589	A1	20020103	US 2001-789017		20010220
US 6607725	B2	20030819			
US 2004126381	A1	20040701	US 2003-688115		20031017
PRIORITY APPLN. INFO.:			US 1996-16020P	P	19960423
			US 1997-842409	A3	19970423
			US 1998-71483P	P	19980113
			WO 1999-US590	A1	19990112
			US 2000-610034	A2	20000705
			US 2001-789017	A2	20010220
			US 2001-288695P	P	20010503
			WO 2001-US32331	A1	20011016

AB A conjugate vaccine for Nontypeable Haemophilus influenzae comprising lipooligosaccharide from which esterified fatty acids have been removed conjugated to an immunogenic carrier. The vaccine is useful for prevention of otitis media and respiratory infections in mammals.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2001:215844 CAPLUS

DOCUMENT NUMBER: 134:294257

TITLE: Functional characteristics of a protective monoclonal antibody against serotype A and C **lipooligosaccharides** from **Moraxella catarrhalis**

AUTHOR(S): Hu, Wei-Gang; Chen, Jing; McMichael, John C.; **Gu, Xin-Xing**

CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA

SOURCE: Infection and Immunity (2001), 69(3), 1358-1363
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody (MAb), designated MAb 8E7 (IgG3), specific for **Moraxella catarrhalis lipooligosaccharide** (**LOS**) was evaluated for its functional activity in vitro and in a mouse model of colonization. ELISA demonstrated that the MAb 8E7 could be prepared to a high titer against **LOS** of the homologous strain 035E, and that it had bactericidal activity. MAb 8E7 reacted with **M. catarrhalis** serotype A and C LOSs but not serotype B **LOS**, as measured by ELISA and Western blotting. On the basis of published structures of LOSs, this suggests that the epitope recognized by MAb 8E7 is directed to a common sequence of either α-GlcNAc-(1→2)-β-Glc-(1→at the branch substituting position 4 of the trisubstituted Glc residue or a terminal tetrasaccharide α-Gal-(1→4)-β-Gal-(1→4)-α-Glc-(1→2)-β-Glc-(1 → at the branch substituting position 6 of the trisubstituted Glc residue. In a whole-cell ELISA, MAb 8E7 reacted with 70% of the 30 wild-type strains and clin. isolates tested. Immuno-electron microscopy demonstrated that MAb 8E7 reacted with a cell surface-exposed epitope of **LOS** on strain O35E. MAb 8E7

inhibited the adherence of strain O35E to Chang conjunctival epithelial cells by 90%. Passive immunization with MAb 8E7 could significantly enhance the clearance of strain O35E from mouse lungs in an aerosol challenge mouse model. This enhanced bacterial clearance was inhibited when MAb 8E7 was absorbed by **M. catarrhalis** serotype A **LOS**, indicating that the **M. catarrhalis** **LOS**-directed antibody may play a major role in the enhancement of **M. catarrhalis** clearance from lungs. These data suggest that MAb 8E7, which recognizes surface-exposed **LOS** of **M. catarrhalis**, is a protective antibody against **M. catarrhalis**.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 14 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:223209 BIOSIS
DOCUMENT NUMBER: PREV200200223209
TITLE: A new intra-NALT injection route in mice enhances mucosal and systemic immune responses against **Moraxella catarrhalis**.
AUTHOR(S): Hou, Y. [Reprint author]; Hu, W. [Reprint author]; Hirano, T. [Reprint author]; **Gu, X.** [Reprint author]
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 342. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002

AB Mucosally administered antigens are often poorly immunogenic. The poor transport of vaccine candidates through the mucosal epithelium is likely one of major factors influencing the weak immune response. We investigated intra-nasal-associated lymphoid tissue (NALT) injections of antigen to circumvent transportation of vaccine candidates through intranasal epithelium. A comparative study was carried out on mice administered with whole cells of **Moraxella catarrhalis** strain 25238 by intra-NALT injection and intranasal dropping. Both routes induced a significant rise of immunoglobulin (Ig) A, IgG, and IgM against **M. catarrhalis** whole cells and **lipooligosaccharides** (**LOS**) in serum, saliva and lungs as measured by an enzyme-linked immunosorbent assay. However, these antibody levels were significantly higher in the intra-NALT injection group than those in the intranasal dropping group. In addition, IgA, IgG, and IgM secreting cells were significantly increased in the intra-NALT injection group as compared to those in the intranasal dropping group. Both routes generated significant reductions of bacteria in the lungs when compared with the control groups following an aerosol challenge with strain 25238. Furthermore, intra-NALT injection showed better bacterial clearance relative to that of intranasal dropping. These results demonstrate that

intra-NALT injection is an effective route for mucosal immunization to elicit both improved mucosal and systemic immune responses.

L31 ANSWER 15 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:201461 BIOSIS
DOCUMENT NUMBER: PREV200200201461
TITLE: Intranasal immunization with detoxified **lipooligosaccharides** from **Moraxella catarrhalis** conjugated to a protein elicit protection in a mouse model of colonization.
AUTHOR(S): Jiao, X. [Reprint author]; Hirano, T. [Reprint author]; Hou, Y. [Reprint author]; **Gu, X.** [Reprint author]
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 302. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002

AB **Moraxella catarrhalis** is a significant cause of otitis media in children. **Lipooligosaccharide** (**LOS**) is a major surface antigen of **M. catarrhalis** and a potential vaccine candidate. But little is known about the mucosal immune responses of detoxified **LOS** (**dLOS**)-protein conjugate vaccines and their potential roles on mucosal surfaces. In order to address these issues, BALB/c mice were immunized intranasally with a mixture of **dLOS**-CRM (the diphtheria toxin cross-reactive mutant protein) and cholera toxin (CT) as an adjuvant, **dLOS** plus CT, or CT only. After immunization, the animals were aerosolly challenged with **M. catarrhalis** strain 25238. Immunization with **dLOS**-CRM generated a significant increase in secreting IgA and IgG in nasal washes, bronchoalveolar lavage and saliva, and serum IgG, IgM and IgA against **LOS** of **M. catarrhalis** as detected by an enzyme-linked immunosorbent assay (ELISA). The **dLOS**-CRM elicited **LOS**-specific IgA, IgG, and IgM antibody-forming cells (AFCs) in different lymphoid tissues as measured by an enzyme-linked immunospot (ELISPOT) assay. **LOS**-specific IgA AFCs were found in the nasal passages, spleens, nasal-associated lymphoid tissues (NALT), cervical lymph nodes (CLN), lungs, and small intestines. **LOS**-specific IgG and IgM AFCs were only detected in the spleens, CLN, and nasal passages. Furthermore, the **dLOS**-CRM vaccine generated an 80% bacterial clearance in the nasopharynx and lungs when compared to the controls ($P<0.01$) following an aerosol challenge with the homologous strain 25238. Intriguingly, intranasal immunization with **dLOS**-CRM containing CT showed a higher level of bacterial clearance in both sites when compared to subcutaneous injections with **dLOS**-CRM plus a Ribi adjuvant. These data indicate that **dLOS**-CRM induces specific mucosal and systemic immunity against **M. catarrhalis** through intranasal immunization, and

provides effective bacterial clearance in the mouse nasopharynx and lungs. Therefore, this may be an efficient route for vaccines to prevent otitis media and lower respiratory tract infections caused by **M. catarrhalis**.

L31 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2000:603699 CAPLUS
DOCUMENT NUMBER: 133:280265
TITLE: Enhancement of clearance of bacteria from murine lungs by immunization with detoxified **lipooligosaccharide** from **Moraxella catarrhalis** conjugated to proteins
AUTHOR(S): Hu, Wei-Gang; Chen, Jing; Battey, James F.; **Gu, Xin-Xing**
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, 20850, USA
SOURCE: Infection and Immunity (2000), 68(9), 4980-4985
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Moraxella catarrhalis** strain 25238 detoxified **lipooligosaccharide** (**dLOS**)-protein conjugates induced a significant rise of bactericidal anti-**LOS** antibodies in animals. This study reports the effect of active or passive immunization with the conjugates or their antiserum on pulmonary clearance of **M. catarrhalis** in an aerosol challenge mouse model. Mice were injected s.c. with **dLOS**-tetanus toxoid (**dLOS**-TT), **dLOS**-high-mol.-weight proteins (**dLOS**-HMP) from nontypeable Haemophilus influenzae (NTHi), or nonconjugated materials in Ribi adjuvant and then challenged with **M. catarrhalis** strain 25238 or O35E or NTHi strain 12. Immunization with **dLOS**-TT or **dLOS**-HMP generated a significant rise of serum anti-**LOS** IgG and 68% and 35 to 41% redns. of bacteria in lungs compared with the control following challenge with homologous strain 25238 and heterologous strain O35E, resp. Serum anti-**LOS** antibody levels correlated with its bactericidal titers against **M. catarrhalis** and bacterial CFU in lungs. Addnl., immunization with **dLOS**-HMP generated a 54% reduction of NTHi strain 12 compared with the control. Passive immunization with a rabbit antiserum against **dLOS**-TT conferred a significant reduction of strain 25238 CFU in lungs in a dose- and time-dependent pattern compared with preimmune serum-treated mice. Kinetic examination of lung tissue sections demonstrated that antiserum-treated mice initiated and offset inflammatory responses more rapidly than preimmune serum-treated mice. These data indicate that **LOS** antibodies (whether active or passive) play a major role in the enhancement of pulmonary clearance of different test strains of **M. catarrhalis** in mice. In addition, **dLOS**-HMP is a potential candidate for a bivalent vaccine against **M. catarrhalis** and NTHi infections.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2000:75871 CAPLUS
DOCUMENT NUMBER: 133:41803
TITLE: Biological activities of antibodies elicited by lipooligosaccharide based-conjugate vaccines of nontypeable Haemophilus influenzae in an otitis media model
AUTHOR(S): Sun, Jianzhong; Chen, Jing; Cheng, Zhengyi; **Robbins, John B.**; Battey, James F.; **Gu, Xin-Xing**
CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA
SOURCE: Vaccine (2000), 18(13), 1264-1272
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vaccination of chinchillas with nontypeable Haemophilus influenzae (NTHi) lipooligosaccharide (LOS) conjugates protected against otitis media. Correlations between the levels of conjugate-induced LOS antibodies (Abs) in sera and middle ear fluids (MEFs) and Ab-mediated biol. functions and protection were examined Following parenteral vaccination and middle ear challenge, all vaccinated animals, but none of the controls, had high titers of anti-LOS in their sera and MEFs. There was a correlation between the levels of anti-LOS IgG + M, IgG or IgA in the sera and in the MEFs. An inverse correlation was found between the level of serum IgG + M and bacterial counts and between the levels of MEF Abs and bacterial counts at the early postchallenge stage. Of the 39 vaccinated animals, 44% showed complete protection against otitis media, 46% (18/39) of their sera inhibited adherence of NTHi to human epithelial cells, 49% (19/39) demonstrated bactericidal activity and 49% (19/39) showed opsonophagocytic activity. In contrast, none of the controls (19) were protected, none of their sera inhibited bacterial adherence or had bactericidal activity and only 21% showed opsonophagocytosis. Our interpretation is that vaccine-induced LOS Abs transuded into the middle ear and conferred immunity to NTHi by binding to LOS of NTHi, inhibition of NTHi adherence to epithelial cells and complement-mediated bacteriolysis (or opsonophagocytosis).

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:386220 BIOSIS
DOCUMENT NUMBER: PREV200000386220
TITLE: Evaluation of detoxified **lipooligosaccharide** from **Moraxella catarrhalis** conjugated to proteins as a vaccine in an aerosol challenge mouse model.
AUTHOR(S): Hu, W. G. [Reprint author]; Chen, J. [Reprint author]; **Gu, X. X.** [Reprint author]
CORPORATE SOURCE: National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 300. print.
Meeting Info.: 100th General Meeting of the American

Society for Microbiology. Los Angeles, California, USA. May 21-25, 2000. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002

L31 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1999:464181 CAPLUS
DOCUMENT NUMBER: 131:86860
TITLE: **Lipooligosaccharide**-based vaccine for prevention of Moraxella (**Branhamella**) **catarrhalis** infections in mammals
INVENTOR(S): **Gu, Xin-Xing; Robbins, John B.**
PATENT ASSIGNEE(S): The Government of the United States of America, Department of Health and Human, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936086	A1	19990722	WO 1999-US590	19990112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315746	AA	19990722	CA 1999-2315746	19990112
AU 9922212	A1	19990802	AU 1999-22212	19990112
BR 9906902	A	20001017	BR 1999-6902	19990112
EP 1047447	A1	20001102	EP 1999-902170	19990112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002509115	T2	20020326	JP 2000-539859	19990112
US 6685949	B1	20040203	US 2000-610034	20000705
US 2004126381	A1	20040701	US 2003-688115	20031017
US 2004115214	A1	20040617	US 2003-729027	20031205

PRIORITY APPLN. INFO.:

US 1998-71483P	P	19980113
US 1996-16020P	P	19960423
US 1997-842409	A3	19970423
WO 1999-US590	W	19990112
US 2000-610034	A2	20000705
US 2001-789017	A2	20010220
US 2001-288695P	P	20010503
WO 2001-US32331	A1	20011016

AB A conjugate vaccine for **Moraxella catarrhalis**

comprising isolated **lipooligosaccharide** from which esterified fatty acids have been removed, to produce a detoxified **lipooligosaccharide** (**dLOS**), or from which lipid A has been removed, to produce a detoxified **oligosaccharide** (**OS**), which is linked to an immunogenic carrier. The immunogenic carrier is selected from the group consisting of UspA or CD derived from **M. catarrhalis**, tetanus toxoid, HMP derived from Haemophilus influenza, diphtheria toxoid, detoxified P. aeruginosa toxin A, cholera toxin, pertussis toxin, hepatitis B surface or core antigen, rotavirus VP 7 protein, CRM, CRM197, CRM3201 and respiratory syncytial virus F and G protein. The vaccine is useful for preventing otitis media and respiratory infections caused by **M. catarrhalis** in mammals, including humans.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 1998:296912 CAPLUS

DOCUMENT NUMBER: 129:53186

TITLE: Synthesis and characterization of **lipooligosaccharide**-based conjugates as vaccine candidates for Moraxella (**Branhamella**) **catarrhalis**

AUTHOR(S): **Gu, Xin-Xing**; Chen, Jing; Barenkamp, Stephen J.; **Robbins, John B.**; Tsai, Chao-Ming; Lim, David J.; Battey, James

CORPORATE SOURCE: Laboratory of Immunology, National Institute on Deafness and Other Communication Disorders, Rockville, MD, 20850, USA

SOURCE: Infection and Immunity (1998), 66(5), 1891-1897
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Moraxella (**Branhamella**) **catarrhalis** is an important cause of otitis media and sinusitis in children and of lower respiratory tract infections in adults. **Lipooligosaccharide** (**LOS**) is a major surface antigen of the bacterium and elicits bactericidal antibodies. Treatment of the **LOS** from strain ATCC 25238 with anhydrous hydrazine reduced its toxicity 20,000-fold, as assayed in the Limulus amebocyte lysate (LAL) test. The detoxified **LOS** (**dLOS**) was coupled to tetanus toxoid (TT) or high-mol.-weight proteins (HMP) from nontypeable Haemophilus influenzae through a linker of adipic acid dihydrazide to form **dLOS**-TT or **dLOS**-HMP. The molar ratios of **dLOS** to TT and HMP conjugates were 19:1 and 31:1, resp. The antigenicity of the two conjugates was similar to that of the **LOS**, as determined by double immunodiffusion. S.c. or i.m. injection of both conjugates elicited a 50- to 100-fold rise in the geometric mean of IgG to the homologous **LOS** in mice after three injections and a 350- to 700-fold rise of anti-**LOS** IgG in rabbits after two injections. The immunogenicity of the conjugate was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced antisera had complement-mediated bactericidal activity against the homologous strain and heterologous strains of **M. catarrhalis**. These results indicate that a detoxified **LOS**-protein conjugate is a

candidate for immunization against **M. catarrhalis** diseases.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 23 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:416635 BIOSIS
DOCUMENT NUMBER: PREV199800416635
TITLE: Characterization of **lipooligosaccharide**-based conjugates as vaccine candidates for moraxella (**Branhamella**) **catarrhalis**.
AUTHOR(S): Chen, J.; **Gu, X-X.**
CORPORATE SOURCE: NIDCD/NIH, Rockville, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1998) Vol. 98, pp. 236. print.
Meeting Info.: 98th General Meeting of the American Society for Microbiology. Atlanta, Georgia, USA. May 17-21, 1998. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 1998
Last Updated on STN: 2 Oct 1998

L31 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1997:730366 CAPLUS
DOCUMENT NUMBER: 128:21619
TITLE: Detoxified lipooligosaccharide from nontypeable Haemophilus influenzae conjugated to proteins confers protection against otitis media in chinchillas
AUTHOR(S): **Gu, Xin-Xing**; Sun, Jianzhong; Jin, Sunji; Barenkamp, Stephen J.; Lim, David J.; **Robbins, John B.**; Battey, James
CORPORATE SOURCE: Lab. Immunology, National Inst. Deafness & Other Communication Disorders, Rockville, MD, 20850, USA
SOURCE: Infection and Immunity (1997), 65(11), 4488-4493
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Detoxified-lipooligosaccharide (dLOS)-protein conjugates from nontypeable Haemophilus influenzae (NTHi) elicited a significant rise of anti-LOS antibodies with bactericidal activity in rabbits (Gu, X.-X., et al., 1996). In this study, we evaluated whether vaccination with the conjugates would protect against NTHi otitis media in chinchillas. Fifty-eight chinchillas received three s.c. or i.m. injections of dLOS-conjugated tetanus toxoid, dLOS-conjugated high-mol.-weight proteins from NTHi, or saline (control) in Freund's adjuvant and then were challenged by intrabullar inoculation with 140 CFU of NTHi. All vaccinated animals responded with elevated serum titers of anti-LOS antibody, and 49% (19 of 39) demonstrated bactericidal activity against the homologous strain. Otitis media with culture-pos. NTHi effusions developed in all 19 controls and 56% (22 of 39) of the vaccinated animals during a period of 21 days. Bacterial counts of the middle ear effusions

were lower in the vaccine groups than in the controls. The incidences of infection in the unchallenged ear or inner ear were 26 or 28% in the vaccine groups and 53 or 58% in the controls. The signs of infection observed by otoscopy were less severe in the vaccine groups than in the controls. There was no significant difference between the two vaccine groups. These data indicate that active immunization with LOS-based conjugates reduces the incidence of NTHi-induced otitis media.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1996:606388 CAPLUS
DOCUMENT NUMBER: 125:245149
TITLE: Synthesis, characterization, and immunologic properties of detoxified lipooligosaccharide from nontypeable Haemophilus influenzae conjugated to proteins
AUTHOR(S): **Gu, Xin-Xing**; Tsai, Chao-Ming; Ueyama, Tomoyo; Barenkamp, Stephen J.; **Robbins, John B.**; Lim, David J.
CORPORATE SOURCE: Vaccine Development Unit, Laboratory Cellular Biology, National Institute Deafness Communication Disorders, Rockville, MD, 20850, USA
SOURCE: Infection and Immunity (1996), 64(10), 4047-4053
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nontypeable Haemophilus influenzae (NTHi) is an important cause of otitis media in children and of pneumonitis in adults with depressed resistance. Lipooligosaccharide (LOS) is a major surface antigen of NTHi and elicits bactericidal and opsonic antibodies. We prepared detoxified LOS (dLOS) protein conjugates from NTHi for use as exptl. vaccines. LOS from NTHi 9274 was treated with anhydrous hydrazine and had its toxicity reduced to clin. acceptable levels. DLOS was bound to tetanus toxoid (TT) or high-mol.-weight proteins (HMPs) from NTHi through a linker of adipic acid dihydrazide to form dLOS-TT or dLOS-HMP. The molar ratio of the dLOS to protein carriers ranged from 26:1 to 50:1. The antigenicity of the conjugates was similar to that of the LOS alone as determined by double immunodiffusion. S.c. or i.m. injection of the conjugates elicited a 28- to 486-fold rise in the level of IgG antibodies in mice to the homologous LOS after two or three injections and a 169- to 243-fold rise in the level of IgG antibodies in rabbits after two injections. The immunogenicity of the conjugates in mice and rabbits was enhanced by formulation with monophosphoryl lipid A plus trehalose dimycolate. In rabbits, conjugate-induced LOS antibodies induced complement-mediated bactericidal activity against the homologous strain 9274 and prototype strain 3189. These results indicate that a detoxified LOS-protein conjugate is a candidate vaccine for otitis media and pneumonitis caused by NTHi.

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